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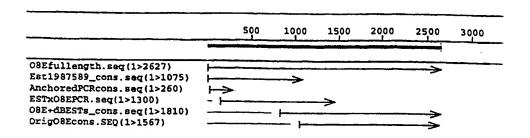
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(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF OVARIAN CANCER



### (57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as ovarian cancer, are disclosed. Compositions may comprise one or more ovarian carcinoma proteins, immunogenic portions thereof, polynucleotides that encode such portions or antibodies or immune system cells specific for such proteins. Such compositions may be used, for example, for the prevention and treatment of diseases such as ovarian cancer. Methods are further provided for identifying tumor antigens that are secreted from ovarian carcinomas and/or other tumors. Polypeptides and polynucleotides as provided herein may further be used for the diagnosis and monitoring of ovarian cancer.

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# COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF OVARIAN CANCER

## TECHNICAL FIELD

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The present invention relates generally to ovarian cancer therapy. The invention is more specifically related to polypeptides comprising at least a portion of an ovarian carcinoma protein, and to polynucleotides encoding such polypeptides, as well as antibodies and immune system cells that specifically recognize such polypeptides. Such polypeptides, polynucleotides, antibodies and cells may be used in vaccines and pharmaceutical compositions for treatment of ovarian cancer.

## 10 BACKGROUND OF THE INVENTION

Ovarian cancer is a significant health problem for women in the United States and throughout the world. Although advances have been made in detection and therapy of this cancer, no vaccine or other universally successful method for prevention or treatment is currently available. Management of the disease currently relies on a combination of early diagnosis and aggressive treatment, which may include one or more of a variety of treatments such as surgery, radiotherapy, chemotherapy and hormone therapy. The course of treatment for a particular cancer is often selected based on a variety of prognostic parameters, including an analysis of specific tumor markers. However, the use of established markers often leads to a result that is difficult to interpret, and high mortality continues to be observed in many cancer patients.

Immunotherapies have the potential to substantially improve cancer treatment and survival. Such therapies may involve the generation or enhancement of an immune response to an ovarian carcinoma antigen. However, to date, relatively few ovarian carcinoma antigens are known and the generation of an immune response against such antigens has not been shown to be therapeutically beneficial.

Accordingly, there is a need in the art for improved methods for identifying ovarian tumor antigens and for using such antigens in the therapy of ovarian cancer. The present invention fulfills these needs and further provides other related advantages.

## SUMMARY OF THE INVENTION

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Briefly stated, this invention provides compositions and methods for the therapy of cancer, such as ovarian cancer. In one aspect, the present invention provides polypeptides comprising an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with ovarian carcinoma protein-specific antisera is not substantially diminished. Within certain embodiments, the ovarian carcinoma protein comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387, 391 and complements of such polynucleotides.

The present invention further provides polynucleotides that encode a polypeptide as described above or a portion thereof, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions and vaccines. Pharmaceutical compositions may comprise a physiologically acceptable carrier or excipient in combination with one or more of: (i) a polypeptide comprising an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with ovarian carcinoma proteinspecific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence encoded by a polynucleotide that comprises a sequence recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391; (ii) a polynucleotide encoding such a polypeptide; (iii) an antibody that specifically binds to such a polypeptide; (iv) an antigen-presenting cell that expresses such a polypeptide and/or (v) a T cell that specifically reacts with such a polypeptide. Vaccines may comprise a non-specific immune response enhancer in combination with one or more of: (i) a polypeptide comprising an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with ovarian carcinoma protein-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence encoded by a

polynucleotide that comprises a sequence recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391; (ii) a polynucleotide encoding such a polypeptide; (iii) an anti-idiotypic antibody that is specifically bound by an antibody that specifically binds to such a polypeptide; (iv) an antigen-presenting cell that expresses such a polypeptide and/or (v) a T cell that specifically reacts with such a polypeptide.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein or polynucleotide encoding a fusion protein in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, comprising a fusion protein or polynucleotide encoding a fusion protein in combination with a non-specific immune response enhancer.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

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The present invention further provides, within other aspects, methods for stimulating and/or expanding T cells, comprising contacting T cells with (a) a polypeptide comprising an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with ovarian carcinoma protein-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid, sequence encoded by a polynucleotide that comprises a sequence recited in any, one of SEQ ID NOs:1-387 or 391; (b) a polynucleotide encoding such a polypeptide and/or (c) an antigen presenting cell that expresses such a polypeptide under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Such polypeptide, polynucleotide and/or antigen presenting cell(s) may be present within a pharmaceutical composition or vaccine, for use in stimulating and/or expanding T cells in a mammal.

Within other aspects, the present invention provides methods for inhibiting the development of ovarian cancer in a patient, comprising administering to a patient T cells prepared as described above.

Within further aspects, the present invention provides methods for inhibiting the development of ovarian cancer in a patient, comprising the steps of: (a) incubating CD4+ and/or CD8+ T cells isolated from a patient with one or more of: (i) a polypeptide comprising an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with ovarian carcinoma protein-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence encoded by a polynucleotide that comprises a sequence recited in any one of SEQ ID NOs: 1-387 or 391; (ii) a polynucleotide encoding such a polypeptide; or (iii) an antigen-presenting cell that expresses such a polypeptide; such that T-cells proliferate; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of ovarian cancer in the patient. The proliferated cells may be cloned prior to administration to the patient.

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The present invention also provides, within other aspects. methods for identifying secreted tumor antigens. Such methods comprise the steps of: (a) implanting tumor cells in an immunodeficient mammal; (b) obtaining serum from the immunodeficient mammal after a time sufficient to permit secretion of tumor antigens into the serum; (c) immunizing an immunocompetent mammal with the serum; (d) obtaining antiserum from the immunocompetent mammal; and (e) screening a tumor expression library with the antiserum, and therefrom identifying a secreted tumor antigen. A preferred method for identifying a secreted ovarian carcinoma antigen comprises the steps of: (a) implanting ovarian carcinoma cells in a SCID mouse; (b) obtaining serum from the SCID mouse after a time sufficient to permit secretion of ovarian carcinoma antigens into the serum; (c) immunizing an immunocompetent mouse with the serum; (d) obtaining antiserum from the immunocompetent mouse; and (e) screening an ovarian carcinoma expression library with the antiserum, and therefrom identifying a secreted ovarian carcinoma antigen.

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These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

## BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A-1S (SEQ ID NOs:1-71) depict partial sequences of polynucleotides encoding representative secreted ovarian carcinoma antigens.

Figure 2A-2C depict full insert sequences for three of the clones of Figure 1. Figure 2A shows the sequence designated O7E (11731; SEQ ID NO:72), Figure 2B shows the sequence designated O9E (11785; SEQ ID NO:73) and Figure 2C shows the sequence designated O8E (13695; SEQ ID NO:74).

Figure 3 presents results of microarray expression analysis of the ovarian carcinoma sequence designated O8E.

Figure 4 presents a partial sequence of a polynucleotide (designated 3g; SEQ ID NO:75) encoding an ovarian carcinoma sequence that is a splice fusion between the human T-cell leukemia virus type I oncoprotein TAX and osteonectin.

Figure 5 presents the ovarian carcinoma polynucleotide designated 3f (SEQ ID NO:76).

Figure 6 presents the ovarian carcinoma polynucleotide designated 6b (SEQ ID NO:77).

Figures 7A and 7B present the ovarian carcinoma polynucleotides designated 8e (SEQ ID NO:78) and 8h (SEQ ID NO:79).

Figure 8 presents the ovarian carcinoma polynucleotide designated 12c (SEQ ID NO:80).

Figure 9 presents the ovarian carcinoma polynucleotide designated 12h (SEQ ID NO:81).

Figure 10 depicts results of microarray expression analysis of the ovarian carcinoma sequence designated 3f.

Figure 11 depicts results of microarray expression analysis of the ovarian carcinoma sequence designated 6b.

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Figure 12 depicts results of microarray expression analysis of the ovarian carcinoma sequence designated 8e.

Figure 13 depicts results of microarray expression analysis of the ovarian carcinoma sequence designated 12c.

Figure 14 depicts results of microarray expression analysis of the ovarian carcinoma sequence designated 12h.

Figures 15A-15EEE depict partial sequences of additional polynucleotides encoding representative secreted ovarian carcinoma antigens (SEQ ID NOs:82-310).

Figure 16 is a diagram illustrating the location of various partial O8E sequences within the full length sequence.

## DETAILED DESCRIPTION OF THE INVENTION

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As noted above, the present invention is generally directed to compositions and methods for the therapy of cancer, such as ovarian cancer. The compositions described herein may include immunogenic polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies that bind to a polypeptide, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells).

Polypeptides of the present invention generally comprise at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof. Certain ovarian carcinoma proteins have been identified using an immunoassay technique, and are referred to herein as ovarian carcinoma antigens. An "ovarian carcinoma antigen" is a protein that is expressed by ovarian tumor cells (preferably human cells) at a level that is at least two fold higher than the level in normal ovarian cells. Certain ovarian carcinoma antigens react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera generated against serum from an immunodeficient animal implanted with a human ovarian tumor. Such ovarian carcinoma antigens are shed or secreted from an ovarian tumor into the sera of the immunodeficient animal. Accordingly, certain ovarian carcinoma antigens provided herein are secreted antigens. Certain nucleic acid sequences of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence.

The present invention further provides ovarian carcinoma sequences that are identified using techniques to evaluate altered expression within an ovarian tumor. Such sequences may be polynucleotide or protein sequences. Ovarian carcinoma sequences are generally expressed in an ovarian tumor at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in normal ovarian tissue, as determined using a representative assay provided herein. Certain partial ovarian carcinoma polynucleotide sequences are presented herein. Proteins encoded by genes comprising such polynucleotide sequences (or complements thereof) are also considered ovarian carcinoma proteins.

Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to at least a portion of an ovarian carcinoma polypeptide as described herein. T cells that may be employed within the compositions provided herein are generally T cells (e.g., CD4<sup>-</sup> and/or CD8<sup>-</sup>) that are specific for such a polypeptide. Certain methods described herein further employ antigen-presenting cells (such as dendritic cells or macrophages) that express an ovarian carcinoma polypeptide as provided herein.

## 20 OVARIAN CARCINOMA POLYNUCLEOTIDES

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Any polynucleotide that encodes an ovarian carcinoma protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides, and more preferably at least 45 consecutive nucleotides, that encode a portion of an ovarian carcinoma protein. More preferably, a polynucleotide encodes an immunogenic portion of an ovarian carcinoma protein, such as an ovarian carcinoma antigen. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a

polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes an ovarian carcinoma protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native ovarian carcinoma protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native ovarian carcinoma protein or a portion thereof.

The percent identity for two polynucleotide or polypeptide sequences may be readily determined by comparing sequences using computer algorithms well known to those of ordinary skill in the art, such as Megalign, using default parameters. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, or 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Optimal alignment of sequences for comparison may be conducted, for example, using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. Preferably, the percentage of sequence identity is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the window may comprise additions or deletions (i.e., gaps) of 20 % or less, usually 5 to 15 %, or 10 to 12%, relative to the reference sequence (which does not contain additions or deletions). The percent identity may be calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched

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positions by the total number of positions in the reference sequence (i.e., the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native ovarian carcinoma protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

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It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, an ovarian carcinoma polynucleotide may be identified, as described in more detail below, by screening a late passage ovarian tumor expression library with antisera generated against sera of immunocompetent mice after injection of such mice with sera from SCID mice implanted with late passage ovarian tumors. Ovarian carcinoma polynucleotides may also be identified using any of a variety of techniques designed to evaluate differential gene expression. Alternatively, polynucleotides may be amplified from cDNA prepared from ovarian tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific

primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (e.g., an ovarian carcinoma cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

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For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with <sup>32</sup>P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be

sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (see Triglia et al., Nucl. Acids Res. 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Additional techniques include capture PCR (Lagerstrom et al., PCR Methods Applic. 1:111-19, 1991) and walking PCR (Parker et al., Nucl. Acids. Res. 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding portions of ovarian carcinoma antigens are provided in Figures 1A-1S (SEQ ID NOS:1 to 71) and Figures 15A to 15EEE (SEQ ID NOS:82 to 310). The sequences provided in Figures 1A-1S appear to be novel. For sequences in Figures 15A-15EEE, database searches revealed matches having substantial identity. These polynucleotides were isolated by serological screening of an ovarian tumor cDNA expression library, using a technique designed to identify secreted tumor antigens. Briefly, a late passage ovarian tumor expression library was prepared from a SCID-derived human ovarian tumor (OV9334) in the vector  $\lambda$ -screen (Novagen). The sera used for screening were obtained by injecting immunocompetent mice with sera from SCID mice implanted with one late

passage ovarian tumors. This technique permits the identification of cDNA molecules that encode immunogenic portions of secreted tumor antigens.

The polynucleotides recited herein, as well as full length polynucleotides comprising such sequences, other portions of such full length polynucleotides, and sequences complementary to all or a portion of such full length molecules, are specifically encompassed by the present invention. It will be apparent to those of ordinary skill in the art that this technique can also be applied to the identification of antigens that are secreted from other types of tumors.

Other nucleic acid sequences of cDNA molecules encoding portions of ovarian carcinoma proteins are provided in Figures 4-9 (SEQ ID NOs:75-81), as well as SEQ ID NOs:313-384. These sequences were identified by screening a microarray of cDNAs for tumor-associated expression (i.e., expression that is at least five fold greater in an ovarian tumor than in normal ovarian tissue, as determined using a representative assay provided herein). Such screens were performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997). SEQ ID NOs:311 and 391 provide full length sequences incorporating certain of these nucleic acid sequences.

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Any of a variety of well known techniques may be used to evaluate tumor-associated expression of a cDNA. For example, hybridization techniques using labeled polynucleotide probes may be employed. Alternatively, or in addition, amplification techniques such as real-time PCR may be used (see Gibson et al., Genome Research 6:995-1001, 1996; Heid et al., Genome Research 6:986-994, 1996). Real-time PCR is a technique that evaluates the level of PCR product accumulation during amplification. This technique permits quantitative evaluation of mRNA levels in multiple samples. Briefly, mRNA is extracted from tumor and normal tissue and cDNA is prepared using standard techniques. Real-time PCR may be performed, for example, using a Perkin Elmer/Applied Biosystems (Foster City, CA) 7700 Prism instrument. Matching primers and fluorescent probes may be designed for genes of interest using, for example, the primer express program provided by Perkin Elmer/Applied Biosystems (Foster City, CA). Optimal concentrations of primers and probes may be initially

determined by those of ordinary skill in the art, and control (e.g., β-actin) primers and probes may be obtained commercially from, for example, Perkin Elmer/Applied Biosystems (Foster City, CA). To quantitate the amount of specific RNA in a sample, a standard curve is generated alongside using a plasmid containing the gene of interest. Standard curves may be generated using the Ct values determined in the real-time PCR, which are related to the initial cDNA concentration used in the assay. Standard dilutions ranging from 10-10<sup>6</sup> copies of the gene of interest are generally sufficient. In addition, a standard curve is generated for the control sequence. This permits standardization of initial RNA content of a tissue sample to the amount of control for comparison purposes.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., DNA 2:183, 1983). Alternatively, RNA molecules may be generated by in vitro or in vivo transcription of DNA sequences encoding an ovarian carcinoma antigen, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated in vivo.

A portion of a sequence complementary to a coding sequence (i.e., an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells or tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of an ovarian carcinoma protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., In Huber and Carr, Molecular and Immunologic Approaches, Futura Publishing Co. (Mt. Kisco, NY; 1994). Alternatively, an antisense molecule

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may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

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Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may

also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

## 10 OVARIAN CARCINOMA POLYPEPTIDES

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Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof, as described herein. As noted above, certain ovarian carcinoma proteins are ovarian carcinoma antigens that are expressed by ovarian tumor cells and react detectably within an immunoassay (such as an ELISA) with antisera generated against serum from an immunodeficient animal implanted with an ovarian tumor. Other ovarian carcinoma proteins are encoded by ovarian carcinoma polynucleotides recited herein. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of an antigen that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of an ovarian carcinoma protein or a variant thereof. Preferred immunogenic portions are encoded by cDNA molecules isolated as described herein. Further immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with ovarian carcinoma protein-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "ovarian carcinoma

protein-specific" if they specifically bind to an ovarian carcinoma protein (*i.e.*, they react with the ovarian carcinoma protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera, antibodies and T cells may be prepared as described herein, and using well known techniques. An immunogenic portion of a native ovarian carcinoma protein is a portion that reacts with such antisera, antibodies and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length protein. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

As noted above, a composition may comprise a variant of a native ovarian carcinoma protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native ovarian carcinoma protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with ovarian carcinoma protein-specific antisera may be enhanced or unchanged, relative to the native ovarian carcinoma protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native ovarian carcinoma protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with ovarian carcinoma protein-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity to the native polypeptide. Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

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Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host

cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, J. Am. Chem. Soc. 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Applied BioSystems, Inc. (Foster City, CA), and may be operated according to the manufacturer's instructions.

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Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises one polypeptide as described herein and a known tumor antigen, such as an ovarian carcinoma protein or a variant of such a protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a

recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

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A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., Gene 40:39-46, 1985; Murphy et al., Proc. Natl. Acad. Sci. USA 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in E. coli (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen present cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemaglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

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In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the LytA gene; *Gene 43*:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology 10*:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

### 10 BINDING AGENTS

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The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to an ovarian carcinoma protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to an ovarian carcinoma protein if it reacts at a detectable level (within, for example, an ELISA) with an ovarian carcinoma protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a "complex" is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10<sup>3</sup> L/mol. The binding constant maybe determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as ovarian cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a ovarian carcinoma antigen will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological

samples (e.g., blood, sera, leukophoresis, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

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Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, Eur. J. Immunol. 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the

desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

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Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include <sup>90</sup>Y, <sup>123</sup>I, <sup>125</sup>I, <sup>131</sup>I, <sup>186</sup>Re, <sup>188</sup>Re, <sup>211</sup>At, and <sup>212</sup>Bi. Preferred drugs include

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methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diptheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of

derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

Also provided herein are anti-idiotypic antibodies that mimic an immunogenic portion of an ovarian carcinoma protein. Such antibodies may be raised against an antibody, or antigen-binding fragment thereof, that specifically binds to an

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immunogenic portion of an ovarian carcinoma protein, using well known techniques. Anti-idiotypic antibodies that mimic an immunogenic portion of an ovarian carcinoma protein are those antibodies that bind to an antibody, or antigen-binding fragment thereof, that specifically binds to an immunogenic portion of an ovarian carcinoma protein, as described herein.

## T CELLS

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Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for an ovarian carcinoma protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be present within (or isolated from) bone marrow, peripheral blood or a fraction of bone marrow or peripheral blood of a mammal, such as a patient, using a commercially available cell separation system, such as the CEPRATE™ system, available from CellPro Inc., Bothell WA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human animals, cell lines or cultures.

T cells may be stimulated with an ovarian carcinoma polypeptide, polynucleotide encoding an ovarian carcinoma polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, an ovarian carcinoma polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for an ovarian carcinoma polypeptide if the T cells kill target cells coated with an ovarian carcinoma polypeptide or expressing a gene encoding such a polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., Cancer Res. 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be

accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with an ovarian carcinoma polypeptide (200 ng/ml - 100  $\mu$ g/ml, preferably 100 ng/ml - 25  $\mu$ g/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells and/or contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998). T cells that have been activated in response to an ovarian carcinoma polypeptide, polynucleotide or ovarian carcinoma polypeptide-expressing APC may be CD4+ and/or CD8+. Ovarian carcinoma polypeptide-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from a patient or a related or unrelated donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to an ovarian carcinoma polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to an ovarian carcinoma polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize an ovarian carcinoma polypeptide. Alternatively, one or more T cells that proliferate in the presence of an ovarian carcinoma polypeptide can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution. Following expansion, the cells may be administered back to the patient as described, for example, by Chang et al., *Crit. Rev. Oncol. Hematol.* 22:213, 1996.

## PHARMACEUTICAL COMPOSITIONS AND VACCINES

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Within certain aspects, polypeptides, polynucleotides, binding agents and/or immune system cells as described herein may be incorporated into

pharmaceutical compositions or vaccines. Pharmaceutical compositions comprise one or more such compounds or cells and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds or cells and a non-specific immune response enhancer. A non-specific immune response enhancer may be any substance that enhances an immune response to an exogenous antigen. Examples of non-specific immune response enhancers include adjuvants, biodegradable microspheres (e.g., polylactic galactide) and liposomes (into which the compound is incorporated; see e.g., Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound within the composition or vaccine.

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A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated in situ. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as Bacillus-Calmette-Guerrin) that expresses an immunogenic portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., PNAS 86:317-321, 1989; Flexner et al., Ann. N.Y. Acad. Sci. 569:86-103, 1989; Flexner et al., Vaccine 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, Biotechniques 6:616-627, 1988; Rosenfeld et al., Science 252:431-434, 1991; Kolls et al., PNAS 91:215-219, 1994; Kass-Eisler et al.,

PNAS 90:11498-11502, 1993; Guzman et al., Circulation 88:2838-2848, 1993; and Guzman et al., Cir. Res. 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., Science 259:1745-1749, 1993 and reviewed by Cohen, Science 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

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Any of a variety of non-specific immune response enhancers may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune

responses, such as lipid A. Bortadella pertussis or Mycobacterium tuberculosis derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI), Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ), alum, biodegradable microspheres, monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN-γ, IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6, IL-10 and TNF-β) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, Ann. Rev. Immunol. 7:145-173, 1989.

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Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). Also preferred is AS-2 (SmithKline Beecham). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO

96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (i.e., a formulation such as a capsule or sponge that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages. B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

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Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent

APCs (Banchereau and Steinman, *Nature 392*:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med. 50*:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*) and based on the lack of differentiation markers of B cells (CD19 and CD20), T cells (CD3), monocytes (CD14) and natural killer cells (CD56), as determined using standard assays. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see Zitvogel et al.*, *Nature Med. 4*:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated  $ex\ vivo$  by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcy receptor, mannose receptor and DEC-205 marker. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell

activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80 and CD86).

APCs may generally be transfected with a polynucleotide encoding a ovarian carcinoma antigen (or portion or other variant thereof) such that the antigen, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place ex vivo, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs in vivo. In vivo and ex vivo transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., Immunology and cell Biology 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

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#### **CANCER THERAPY**

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as ovarian cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Within certain preferred embodiments, a patient is afflicted with ovarian cancer. Such cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or

following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immuno response-modifying agents (such as tumor vaccines, bacterial adjuvants and/or cytokines).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

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Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example,

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antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow in vivo and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., Immunological Reviews 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into stem cells taken from a patient and clonally propagated *in vitro* for autologous transplant back into the same patient.

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Routes and frequency of administration, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration), orally or in the bed of a resected tumor. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (i.e., untreated) level.. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells in vitro. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 100 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to an ovarian carcinoma antigen generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

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# SCREENS FOR IDENTIFYING SECRETED OVARIAN CARCINOMA ANTIGENS

The present invention provides methods for identifying secreted tumor antigens. Within such methods, tumors are implanted into immunodeficient animals such as SCID mice and maintained for a time sufficient to permit secretion of tumor antigens into serum. In general, tumors may be implanted subcutaneously or within the gonadal fat pad of an immunodeficient animal and maintained for 1-9 months, preferably 1-4 months. Implantation may generally be performed as described in WO 97/18300. The serum containing secreted antigens is then used to prepare antisera in immunocompetent mice, using standard techniques and as described herein. Briefly,  $50\text{-}100~\mu\text{L}$  of sera (pooled from three sets of immunodeficient mice, each set bearing a different SCID-derived human ovarian tumor) may be mixed 1:1 (vol:vol) with an appropriate adjuvant, such as RIBI-MPL or MPL + TDM (Sigma Chemical Co., St. Louis, MO) and injected intraperitoneally into syngeneic immunocompetent animals at monthly intervals for a total of 5 months. Antisera from animals immunized in such a manner may be obtained by drawing blood after the third, fourth and fifth immunizations. The resulting antiserum is generally pre-cleared of E. coli and phage antigens and used (generally following dilution, such as 1:200) in a serological expression screen.

The library is typically an expression library containing cDNAs from one or more tumors of the type that was implanted into SCID mice. This expression library may be prepared in any suitable vector, such as  $\lambda$ -screen (Novagen). cDNAs that

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encode a polypeptide that reacts with the antiserum may be identified using standard techniques, and sequenced. Such cDNA molecules may be further characterized to evaluate expression in tumor and normal tissue, and to evaluate antigen secretion in patients.

The methods provided herein have advantages over other methods for tumor antigen discovery. In particular, all antigens identified by such methods should be secreted or released through necrosis of the tumor cells. Such antigens may be present on the surface of tumor cells for an amount of time sufficient to permit targeting and killing by the immune system, following vaccination.

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#### METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more ovarian carcinoma proteins and/or polynucleotides encoding such proteins in a biological sample (such as blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as ovarian cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of protein that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, an ovarian carcinoma-associated sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length ovarian carcinoma proteins and portions thereof to which the binding agent binds, as described above.

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The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about

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 $10\,\mu g$ , and preferably about  $100\,n g$  to about  $1\,\mu g$ , is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

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In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with ovarian cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve

equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20<sup>TM</sup>. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as ovarian cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., Clinical Epidemiology: A Basic Science for Clinical Medicine, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot

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of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

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In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1µg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use ovarian carcinoma polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such ovarian carcinoma protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with an ovarian carcinoma protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with an ovarian carcinoma protein, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated in vitro for 2-9 days (typically 4 days) at 37°C with an ovarian carcinoma protein (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of ovarian carcinoma protein to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8+ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding an ovarian carcinoma protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of an ovarian carcinoma protein cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the ovarian carcinoma protein. The amplified cDNA is then separated and detected using techniques well

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known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding an ovarian carcinoma protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

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To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding an ovarian carcinoma protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence provided herein. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample such as a biopsy tissue and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, ovarian carcinoma proteins and polynucleotides encoding such proteins may be used as markers for monitoring the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide detected by the binding agent increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple ovarian carcinoma protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

#### DIAGNOSTIC KITS

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The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to an ovarian carcinoma protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively,

contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding an ovarian carcinoma protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding an ovarian carcinoma protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding an ovarian carcinoma protein.

The following Examples are offered by way of illustration and not by way of limitation.

#### **EXAMPLES**

#### Example 1

### Identification of Representative Ovarian Carcinoma Protein cDNAs

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This Example illustrates the identification of cDNA molecules encoding ovarian carcinoma proteins.

Anti-SCID mouse sera (generated against sera from SCID mice carrying late passage ovarian carcinoma) was pre-cleared of E. coli and phage antigens and used at a 1:200 dilution in a serological expression screen. The library screened was made from a SCID-derived human ovarian tumor (OV9334) using a directional RH oligo(dT) priming cDNA library construction kit and the λScreen vector (Novagen). A bacteriophage lambda screen was employed. Approximately 400,000 pfu of the amplified OV9334 library were screened.

196 positive clones were isolated. Certain sequences that appear to be novel are provided in Figures 1A-1S and SEQ ID NOs:1 to 71. Three complete insert sequences are shown in Figures 2A-2C (SEQ ID NOs:72 to 74). Other clones having known sequences are presented in Figures 15A-15EEE (SEQ ID NOs:82 to 310). Database searches identified the following sequences that were substantially identical to the sequences presented in Figures 15A-15EEE.

These clones were further characterized using microarray technology to determine mRNA expression levels in a variety of tumor and normal tissues. Such analyses were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions. PCR amplification products were arrayed on slides, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes and the slides were scanned to measure fluorescence intensity. Data was analyzed using Synteni's provided GEMtools software. The results for one clone (13695, also referred to as O8E) are shown in Figure 3.

#### Example 2

## Identification of Ovarian Carcinoma cDNAs using Microarray Technology

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This Example illustrates the identification of ovarian carcinoma polynucleotides by PCR subtraction and microarray analysis. Microarrays of cDNAs were analyzed for ovarian tumor-specific expression using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997).

A PCR subtraction was performed using a tester comprising cDNA of four ovarian tumors (three of which were metastatic tumors) and a driver of cDNA form five normal tissues (adrenal gland, lung, pancreas, spleen and brain). cDNA fragments recovered from this subtraction were subjected to DNA microarray analysis where the fragments were PCR amplified, adhered to chips and hybridized with fluorescently labeled probes derived from mRNAs of human ovarian tumors and a variety of normal human tissues. In this analysis, the slides were scanned and the fluorescence intensity was measured, and the data were analyzed using Synteni's GEMtools software. In general, sequences showing at least a 5-fold increase in expression in tumor cells (relative to normal cells) were considered ovarian tumor antigens. The fluorescent results were analyzed and clones that displayed increased expression in ovarian tumors were further characterized by DNA sequencing and database searches to determine the novelty of the sequences.

Using such assays, an ovarian tumor antigen was identified that is a splice fusion between the human T-cell leukemia virus type I oncoprotein TAX (see Jin et al., Cell 93:81-91, 1998) and an extracellular matrix protein called osteonectin. A splice junction sequence exists at the fusion point. The sequence of this clone is presented in Figure 4 and SEQ ID NO:75. Osteonectin, unspliced and unaltered, was also identified from such assays independently.

Further clones identified by this method are referred to herein as 3f, 6b, 8e, 8h, 12c and 12h. Sequences of these clones are shown in Figures 5 to 9 and SEQ ID NOs:76 to 81. Microarray analyses were performed as described above, and are presented in Figures 10 to 14. A full length sequence encompassing clones 3f, 6b, 8e and 12h was obtained by screening an ovarian tumor (SCID-derived) cDNA library. This 2996 base pair sequence (designated O772P) is presented in SEQ ID NO:311, and the encoded 914 amino acid protein sequence is shown in SEQ ID NO:312. PSORT analysis indicates a Type 1a transmembrane protein localized to the plasma membrane.

In addition to certain of the sequences described above, this screen identified the following sequences:

Sequence	Comments
OV4vG11 (SEQ ID NO:313)	human clone 1119D9 on chromosome 20p12
OV4vB11 (SEQ ID NO:314)	human UWGC:y14c094 from chromosome 6p21
OV4vD9 (SEQ ID NO:315)	human clone 1049G16 chromosome 20q12-13.2
OV4vD5 (SEQ ID NO:316)	human KIAA0014 gene
OV4vC2 (SEQ ID NO:317)	human KIAA0084 gene
OV4vF3 (SEQ ID NO:318)	human chromosome 19 cosmid R31167
OV4VC1 (SEQ ID NO:319)	novel
OV4vH3 (SEQ ID NO:320)	novel
OV4vD2 (SEQ ID NO:321)	novel
O815P (SEQ ID NO:322)	novel
OV4vC12 (SEQ ID NO:323)	novel
OV4vA4 (SEQ ID NO:324)	novel
OV4vA3 (SEQ ID NO:325)	novel
OV4v2A5 (SEQ ID NO:326)	novel
O819P (SEQ ID NO:327)	novel
O818P (SEQ ID NO:328)	novel
O817P (SEQ ID NO:329)	novel
O816P (SEQ ID NO:330)	novel
Ov4vC5 (SEQ ID NO:331)	novel

Sequence	Comments
21721 (SEQ ID NO:332)	human lumican
21719 (SEQ ID NO:333)	human retinoic acid-binding protein II
21717 (SEQ ID NO:334)	
21654 (SEQ ID NO:335)	human26S proteasome ATPase subunit
•	human copine I
21627 (SEQ ID NO:336)	human neuron specific gamma-2 enolase
21623 (SEQ ID NO:337)	human geranylgeranyl transferase II
21621 (SEQ ID NO:338)	human cyclin-dependent protein kinase
21616 (SEQ ID NO:339)	human prepro-megakaryocyte potentiating factor
21612 (SEQ ID NO:340)	human UPH1
21558 (SEQ ID NO:341)	human RalGDS-like 2 (RGL2)
21555 (SEQ ID NO:342)	human autoantigen P542
21548 (SEQ ID NO:343)	human actin-related protein (ARP2)
21462 (SEQ ID NO:344)	human huntingtin interacting protein
21441 (SEQ ID NO:345)	human 90K product (tumor associated antigen)
21439 (SEQ ID NO:346)	human guanine nucleotide regulator protein (tim1)
21438 (SEQ ID NO:347)	human Ku autoimmune (p70/p80) antigen
21237 (SEQ ID NO:348)	human S-laminin
21436 (SEQ ID NO:349)	human ribophorin I
21435 (SEQ ID NO:350)	human cytoplasmic chaperonin hTRiC5
21425 (SEQ ID NO:351)	humanEMX2
21423 (SEQ ID NO:352)	human p87/p89 gene
21419 (SEQ ID NO:353)	human HPBRII-7
21252 (SEQ ID NO:354)	human T1-227H
21251 (SEQ ID NO:355)	human cullin I
21247 (SEQ ID NO:356)	kunitz type protease inhibitor (KOP)
21244-1 (SEQ ID NO:357)	human protein tyrosine phosphatase receptor F (PTPRF)
21718 (SEQ ID NO:358)	human LTR repeat
OV2-90 (SEQ ID NO:359)	novel

Sequence	Comments	
Human zinc finger (SEQ ID NO:3	360)	
Human polyA binding protein (SE	EQ ID NO:361)	
Human pleitrophin (SEQ ID NO:3	362)	
Human PAC clone 278C19 (SEQ	ID NO:363)	
Human LLRep3 (SEQ ID NO:364	3)	
Human Kunitz type protease inhib	(SEQ ID NO:365)	
Human KIAA0106 gene (SEQ ID	NO:366)	
Human keratin (SEQ ID NO:367)		
Human HIV-1TAR (SEQ ID NO:	368)	
Human glia derived nexin (SEQ II	D NO:369)	
Human fibronectin (SEQ ID NO:3	370)	
Human ECMproBM40 (SEQ ID N	NO:371)	
Human collagen (SEQ ID NO:372	2)	
Human alpha enolase (SEQ ID NO	D:373)	
Human aldolase (SEQ ID NO:374	)	
Human transf growth factor BIG H3 (SEQ ID NO:375)		
Human SPARC osteonectin (SEQ	ID NO:376)	
Human SLP1 leucocyte protease (	SEQ ID NO:377)	
Human mitochondrial ATP synth	(SEQ ID NO:378)	
Human DNA seq clone 461P17 (S	SEQ ID NO:379)	
Human dbpB pro Y box (SEQ ID	NO:380)	
Human 40 kDa keratin (SEQ ID N	IO:381)	
Human arginosuccinate synth (SE	Q ID NO:382)	
Human acidic ribosomal phosphoprotein (SEQ ID NO:383)		
Human colon carcinoma laminin b	pinding pro (SEQ ID NO:384)	

This screen further identified multiple forms of the clone O772P, referred to herein as 21013, 21003 and 21008. PSORT analysis indicates that 21003 (SEQ ID NO:386; translated as SEQ ID NO:389) and 21008 (SEQ ID NO:387; translated as SEQ ID NO:390) represent Type 1a transmembrane protein forms of

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O772P. 21013 (SEQ ID NO:385; translated as SEQ ID NO:388) appears to be a truncated form of the protein and is predicted by PSORT analysis to be a secreted protein.

Additional sequence analysis resulted in a full length clone for O8E (2627 bp, which agrees with the message size observed by Northern analysis; SEQ ID NO:391). This nucleotide sequence was obtained as follows: the original O8E sequence (OrigO8Econs) was found to overlap by 33 nucleotides with a sequence from an EST clone (IMAGE#1987589). This clone provided 1042 additional nucleotides upstream of the original O8E sequence. The link between the EST and O8E was confirmed by sequencing multiple PCR fragments generated from an ovary primary tumor library using primers to the unique EST and the O8E sequence (ESTxO8EPCR). Full length status was further indicated when anchored PCR from the ovary tumor library gave several clones (AnchoredPCR cons) that all terminated upstream of the putative start methionine, but failed to yield any additional sequence information. Figure 16 presents a diagram that illustrates the location of each partial sequence within the full length O8E sequence.

Two protein sequences may be translated from the full length O8E. For "a" (SEQ ID NO:393) begins with a putative start methionine. A second form "b" (SEQ ID NO:392) includes 27 additional upstream residues to the 5' end of the nucleotide sequence.

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

### SUMMARY OF SEQUENCE LISTING

20

25

SEQ ID NOs:1-71 are ovarian carcinoma antigen polynucleotides shown in Figures 1A-1S.

SEQ ID NOs:72-74 are ovarian carcinoma antigen polynucleotides 30 shown in Figures 2A-2C.

SEQ ID NO:75 is the ovarian carcinoma polynucleotide 3g (Figure 4).

5

15

SEQ ID NO:76 is the ovarian carcinoma polynucleotide 3f (Figure 5).

SEQ ID NO:77 is the ovarian carcinoma polynucleotide 6b (Figure 6).

SEQ ID NO:78 is the ovarian carcinoma polynucleotide 8e (Figure 7A).

SEQ ID NO:79 is the ovarian carcinoma polynucleotide 8h (Figure 7B).

SEQ ID NO:80 is the ovarian carcinoma polynucleotide 12e (Figure 8).

SEQ ID NO:81 is the ovarian carcinoma polynucleotide 12h (Figure 9).

SEQ ID NOs:82-310 are ovarian carcinoma antigen polynucleotides shown in Figures 15A-15EEE.

SEQ ID NO:311 is a full length sequence of ovarian carcinoma 10 polynucleotide O772P.

SEQ ID NO:312 is the O772P amino acid sequence.

SEQ ID NOs:313-384 are ovarian carcinoma antigen polynucleotides.

SEQ ID NOs:385-390 present sequences of O772P forms.

SEQ ID NO:391 is a full length sequence of ovarian carcinoma polynucleotide O8E.

SEQ ID NOs:392-393 are protein sequences encoded by O8E.

#### **CLAIMS**

- 1. An isolated polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigenspecific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) polynucleotides recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391; and
  - (b) complements of the foregoing polynucleotides.
- 2. A polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) polynucleotides recited in any one of 1-81, 313-331, 359, 366, 379, 385-387 or 391; and
  - (b) complements of such polynucleotides.
- 3. An isolated polynucleotide encoding at least 5 amino acid residues of a polypeptide according to claim polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigenspecific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) polynucleotides recited in any one of SEQ ID NOs:1-81, 319-331, 359, 385-387 or 391; and
  - (b) complements of the foregoing polynucleotides

- 4. A polynucleotide according to claim 3, wherein the polynucleotide encodes an immunogenic portion of the polypeptide.
- 5. A polynucleotide according to claim 3, wherein the polynucleotide comprises a sequence recited in any one of SEQ ID NOs:1-81, 319-331, 359, 385-387, 391 or a complement of any of the foregoing sequences.
- 6. An isolated polynucleotide complementary to a polynucleotide according to claim 3.
- 7. An expression vector comprising a polynucleotide according to claim 3 or claim 6.
- A host cell transformed or transfected with an expression vector according to claim 7.
- 9. A pharmaceutical composition comprising a polypeptide according to claim 1, in combination with a physiologically acceptable carrier.
- 10. A pharmaceutical composition according to claim 9, wherein the polypeptide comprises an amino acid sequence encoded by a polynucleotide that comprises a sequence recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391.
- 11. A vaccine comprising a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.
- 12. A vaccine according to claim 11, wherein the polypeptide comprises an amino acid sequence encoded by a polynucleotide that comprises a sequence recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391.
  - 13. A pharmaceutical composition comprising:

- (a) a polynucleotide encoding an ovarian carcinoma polypeptide, wherein the polypeptide comprises at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-81, 319-331, 359, 385-387 or 391; and
  - (ii) complements of the foregoing polynucleotides; and
  - (b) a physiologically acceptable carrier.
- 14. A pharmaceutical composition according to claim 13, wherein the polynucleotide comprises a sequence recited in any one of SEQ ID NOs:1-81, 319-331, 359, 385-387, 391 or a complement of any of the foregoing sequences.
  - 15. A vaccine comprising:
- (a) a polynucleotide encoding an ovarian carcinoma polypeptide, wherein the polypeptide comprises at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391; and
  - (ii) complements of the foregoing polynucleotides; and
- 16. A vaccine according to claim 15, wherein the polynucleotide comprises a sequence recited in any one of SEQ ID NOs:1-81. 319-331, 359, 385-387 or 391.
  - 17. A pharmaceutical composition comprising:

- (a) an antibody that specifically binds to an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391; and
  - (ii) complements of such polynucleotides; and
  - (b) a physiologically acceptable carrier.
- 18. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to a patient an effective amount of an agent selected from the group consisting of:
- (a) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of such polynucleotides;
  - (b) a polynucleotide encoding a polypeptide as recited in (a); and
- (c) an antibody that specifically binds to an ovarian carcinoma protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of such polynucleotides; and thereby inhibiting the development of ovarian cancer in the patient.

- 19. A method according to claim 18, wherein the agent is present within a pharmaceutical composition according to any one of claims 9, 13 or 17.
- 20. A method according to claim 18, wherein the agent is present within a vaccine according to any one of claims 11, 15 or 18.
- 21. A fusion protein comprising at least one polypeptide according to claim 1.
  - 22. A polynucleotide encoding a fusion protein according to claim 21.
- 23. A pharmaceutical composition comprising a fusion protein according to claim 21 in combination with a physiologically acceptable carrier.
- 24. A vaccine comprising a fusion protein according to claim 21 in combination with a non-specific immune response enhancer.
- 25. A pharmaceutical composition comprising a polynucleotide according to claim 22 in combination with a physiologically acceptable carrier.
- 26. A vaccine comprising a polynucleotide according to claim 22 in combination with a non-specific immune response enhancer.
- 27. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 23 or claim 25.
- 28. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 23 or claim 26.

- 29. A pharmaceutical composition, comprising:
- (a) an antigen presenting cell that expresses an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of such polynucleotides; and
  - (b) a pharmaceutically acceptable carrier or excipient.
  - 30. A vaccine, comprising:
- (a) an antigen presenting cell that expresses an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of such polynucleotides; and
  - (b) a non-specific immune response enhancer.
  - 31. A vaccine comprising:
- (a) an anti-idiotypic antibody or antigen-binding fragment thereof that is specifically bound by an antibody that specifically binds to an ovarian carcinoma protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and

- (ii) complements of such polynucleotides; and
- (b) non-specific immune response enhancer.
- 32. A vaccine according to claim 30 or claim 31, wherein the immune response enhancer is an adjuvant.
  - 33. A pharmaceutical composition, comprising:
- (a) a T cell that specifically reacts with an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of such polynucleotides; and
  - (b) a physiologically acceptable carrier.
  - 34. A vaccine, comprising:
- (a) a T cell that specifically reacts with an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of such polynucleotides; and
  - (b) a non-specific immune response enhancer.

- 35. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to the patient an effective amount of a pharmaceutical composition according to claim 29 or claim 33.
- 36. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to the patient an effective amount of a vaccine according to any one of claims 30, 31 or 34.
- 37. A method for stimulating and/or expanding T cells, comprising contacting T cells with:
- (a) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of such polynucleotides;
  - (b) a polynucleotide encoding such a polypeptide; and/or
- (c) an antigen presenting cell that expresses such a polypeptide under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.
- 38. A method according to claim 37, wherein the T cells are cloned prior to expansion.
- 39. A method for stimulating and/or expanding T cells in a mammal, comprising administering to a mammal a pharmaceutical composition comprising:
  - (a) one or more of:
- (i) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one

or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or

complements of such polynucleotides;

(ii) a polynucleotide encoding an ovarian carcinoma polypeptide;

or

391; and

- (iii) an antigen-presenting cell that expresses an ovarian carcinoma polypeptide; and
  - (b) a physiologically acceptable carrier or excipient;and thereby stimulating and/or expanding T cells in a mammal.
- 40. A method for stimulating and/or expanding T cells in a mammal, comprising administering to a mammal a vaccine comprising:

#### (a) one or more of:

(i) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or

391; and

or

complements of such polynucleotides;

- (ii) a polynucleotide encoding an ovarian carcinoma polypeptide;
- (iii) an antigen-presenting cell that expresses an ovarian carcinoma polypeptide; and

- (b) a non-specific immune response enhancer; and thereby stimulating and/or expanding T cells in a mammal.
- 41. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to a patient T cells prepared according to the method of claim 39 or claim 40.
- 42. A method for inhibiting the development of ovarian cancer in a patient, comprising the steps of:
  - (a) incubating CD4<sup>+</sup> T cells isolated from a patient with one or more of:
- (i) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and

complements of such polynucleotides;

- (ii) a polynucleotide encoding an ovarian carcinoma polypeptide; or
- (iii) an antigen-presenting cell that expresses an ovarian carcinoma polypeptide;

such that T cells proliferate; and

- (b) administering to the patient an effective amount of the proliferated T cells, and therefrom inhibiting the development of ovarian cancer in the patient.
- 43. A method for inhibiting the development of ovarian cancer in a patient, comprising the steps of:
  - (a) incubating CD4<sup>+</sup> T cells isolated from a patient with one or more of:

(i) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or

391; and

complements of such polynucleotides;

(ii) a polynucleotide encoding an ovarian carcinoma polypeptide;

or

(iii) an antigen-presenting cell that expresses an ovarian carcinoma polypeptide;

such that T cells proliferate;

- (b) cloning one or more proliferated cells; and
- (c) administering to the patient an effective amount of the cloned T cells.
- 44. A method for inhibiting the development of ovarian cancer in a patient, comprising the steps of:
  - (a) incubating CD8<sup>+</sup> T cells isolated from a patient with one or more of:
- (i) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or

391; and

complements of such polynucleotides;

- (ii) a polynucleotide encoding an ovarian carcinoma polypeptide; or
- (iii) an antigen-presenting cell that expresses an ovarian carcinoma polypeptide;

such that T cells proliferate; and

- (b) administering to the patient an effective amount of the proliferated T cells, and therefrom inhibiting the development of ovarian cancer in the patient.
- 45. A method for inhibiting the development of ovarian cancer in a patient, comprising the steps of:
  - (a) incubating CD8<sup>+</sup> T cells isolated from a patient with one or more of:
- (i) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and

complements of such polynucleotides:

- (ii) a polynucleotide encoding an ovarian carcinoma polypeptide;
- (iii) an antigen-presenting cell that expresses an ovarian carcinoma polypeptide;

such that the T cells proliferate;

or

- (b) cloning one or more proliferated cells; and
- (c) administering to the patient an effective amount of the cloned T cells.
- 46. A method for identifying a secreted tumor antigen, comprising the steps of:

- (a) implanting tumor cells in an immunodeficient mammal;
- (b) obtaining serum from the immunodeficient mammal after a time sufficient to permit secretion of tumor antigens into the serum;
  - (c) immunizing an immunocompetent mammal with the serum;
  - (d) obtaining antiserum from the immunocompetent mammal; and
- (e) screening a tumor expression library with the antiserum, and therefrom identifying a secreted tumor antigen.
- 47. A method according to claim 46, wherein the immunodeficient mammal is a SCID mouse and wherein the immunocompetent mammal is an immunocompetent mouse.
- 48. A method for identifying a secreted ovarian carcinoma antigen, comprising the steps of:
  - (a) implanting ovarian carcinoma cells in a SCID mouse;
- (b) obtaining serum from the SCID mouse after a time sufficient to permit secretion of ovarian carcinoma antigens into the serum;
  - (c) immunizing an immunocompetent mouse with the serum;
  - (d) obtaining antiserum from the immunocompetent mouse; and
- (e) screening an ovarian carcinoma expression library with the antiserum, and therefrom identifying a secreted ovarian carcinoma antigen.
- 49. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with a binding agent that binds to an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 50. A method according to claim 49, wherein the binding agent is an antibody.
- 51. A method according to claim 50, wherein the antibody is a monoclonal antibody.
  - 52. A method according to claim 49, wherein the cancer is ovarian cancer.
- 53. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

- (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 54. A method according to claim 53, wherein the binding agent is an antibody.
- 55. A method according to claim 54, wherein the antibody is a monoclonal antibody.
  - 56. A method according to claim 53, wherein the cancer is ovarian cancer.
- 57. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 58. A method according to claim 57, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

- 59. A method according to claim 57, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
- 60. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of the foregoing polynucleotides:
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 61. A method according to claim 60, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
- 62. A method according to claim 60, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
  - 63. A diagnostic kit, comprising:
- (a) one or more antibodies or antigen-binding fragments thereof that specifically bind to an ovarian carcinoma protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of the foregoing polynucleotides.; and
  - (b) a detection reagent comprising a reporter group.
- 64. A kit according to claim 63, wherein the antibodies are immobilized on a solid support.
- 65. A kit according to claim 63, wherein the solid support comprises nitrocellulose, latex or a plastic material.
- 66. A kit according to claim 63, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.
- 67. A kit according to claim 63, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.
  - 68. A diagnostic kit, comprising:
- (a) an oligonucleotide comprising 10 to 40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
  - (ii) complements of the foregoing polynucleotides; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

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ggaactggtg ggaggicaag tggggaagtt ggtgaatgtg gaataactta cctttgtgct
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aagtgagact caagagtcta ctgctttagt ggcaactaca gaaaactggt qttacccaga
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      <211> 111
      <212> DNA
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gctacccgtg cctggccagc cactggagtt taaaggacag tcatgttggc tccagcctaa
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ggcggcattt tcccccatca gaaagcccgc ggctcctgta cctcaaaata gggcacctgt
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aaagtcagtc agtgaagtct ctgctctaac tggccacccg gggccattgg cntctgacac
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cctgtgttgg atgttgngtc caatccttga acaaacagct ggagaagaac gaggagaccg
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cttccatage ageaacagat gctttggggc taaaaggcat gtcctctgac cttgcaggtg
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cagtattagc atccacatca gacagcctgg tataaccaga gttggtggtt actgattgta
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g
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aatgaangga aagaaactta gaagctcaac aagctgaaga taatcccatc aggcatttcc
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С
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agagcccaag aaatgtagtc ctgttgatat ggttttgctg tgtcccaacc caaatctcat
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ccacagcagt cagttggtca ggccctgctg tagaaggtca cttggctcca ttgcctgctt
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                                                                       461
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      <211> 769
      <212> DNA
      <213> Homo sapien
      <400> 39
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                                                                        60
gatgtcgcct tttcttcttc ttgctttttc tgatgttctg ctcagcatgt tctgggtgct
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totcatctgc atcattcctt tcagatgctg tagcttcttc ctcctctttc tgcctccttt
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tctttttctt ttttttgggg ggcttgctct ctgactgcag ttgaggggcc ccagggtcct
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ggcctttgag acgagccagg aaggcctgct cctgggcctc taggcgagca agcttggcct
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tcattgtgat cccaagacgg gcagccttgt gtgctgttcg cccctcacag gcttggagca
                                                                      360
gcatctcatc agtcagaatc tttggggact tggacccctg gttgtcgtca tcactgcagc
                                                                      420
totocaagto titgtitggo tictocac otgaagtoaa tgtagocato ticacaaact
                                                                      480
                                                                      540
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<400> 42	
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  aaaatcatta attactttca acttaataac taattgacat tootcaaaag agotgtttto
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  aatcctgata ggttctttat tttttcaaaa tatatttgcc atgggatgct aatttgcaat
                                                                        360
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                                                                        451
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        <211> 521
        <212> DNA
        <213> Homo sapien
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 gttccttttt attatgcttc tggatccgaa tttgatgaga tgtttgtggg tgtggggagcc
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 cagaccataa atcaacttct tgctgaaatg gatggtttta aacccaatga aggagttatc
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                                                                        300
 ttttgacatg caagttacag ttccaaggcc agatgtaaaa ggtcgaacag aaattttgaa
                                                                        360
 atggtatctc aataaaataa agtttgatca atcccgttga tccagaaatt atagcctcga
                                                                        420
 ggtactggtg gcttttccgg aagcagagtt gggagaatct t
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                                                                       521
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                                                                       120
 aggttgatct ttgccggaaa geagctggaa gatggdcgca ccctgtctga ctacaacatc
                                                                       180
 cagaaagagt cyaccetgca cetggtgete egteteagag gtgggatgca ratettegtg
                                                                       240
aagaccctga ctggtaagac catcaccctc gaggtggagc ccagtgacac catcgagaat
                                                                       300
gtcaaggcaa agatccaaga taaggaaggc atccctcctg atcagcagag gttgatcttt
                                                                       360
gctgggaaac agctggaaga tggacgcacc ctgtctgact acaacatcca gaaagagtcc
                                                                       420
actotgcact tggtcctgcg cttgaggggg ggtgtctaag tttccccttt taaggtttcm
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acaaattica tigcactiic ciitcaataa agitgiigca ticcc
                                                                       540
                                                                       585
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      <211> 481
      <212> DNA
      <213> Homo sapien
      <400> 46
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                                                                       60
cttcctgcaa atcacacac catgcgggcc acacatacct gctgccctgg agatggggaa
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gtaggagaga tgaatagagg cccatacatt gtacagaagg aggggcaggt gcagataaaa
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gcagcagacc cagcggcagc tgaggtgcat ggagcacggt tggggccggc attgggctga
                                                                      240
gcacctgatg ggcctcatct cgtgaatcct cgaggcagcg ccacagcaga ggagttaagt
                                                                      300
ggcacctggg ccgagcagag caggagactg agggtcagag tggaggctaa gctgccctgg
                                                                      360
aactecteaa tettgeetge eccetagtat gaageeeeet teetgeeeet acaatteetg
                                                                      420
                                                                      480
                                                                      481
```

```
<211> 461
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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qqtacacngc caccacaccc agctaaaatt tttgtatttt ttgtagagac gggatctcgc
                                                                       180
cacgttgccc aggctggtcc catcctgacc tcaagcagat ctgcccacct cagcccccca
                                                                       240
acgtgctagg attacaggcg tgagccaccg cacccagcct ttgttttgct tttaatggaa
                                                                       300
tcaccagttc ccctccgtgt ctcagcagca gctgtgagaa atgctttgca tctgtgacct
                                                                       360
ttatgaaggg gaacttccat gctgaatgag ggtaggatta catgctcctg tttcccqqqq
                                                                       420
gicaagaaag cctcagactc cagcatgata agcagggtga g
                                                                       461
      <210> 48
      <211> 571
      <212> DNA
      <213> Homo sapien
      <400> 48
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                                                                      120
aggatgcatc aagaaggcgg ccgtctgcaa gcgaaggaga ggccgcacca gaaaccgaca
                                                                      180
ccttcatctt ggacttgcag cctctagaac tgagaaaata actgtctgtt ggttaagcca
                                                                      240
cccagtttgt agtattctct tatggcttcc taagcagact aacaaacaaa cacccaaaat
                                                                      300
taactgatgg cttcgctgtc ttctgtaaaa attgctatga qaqaactttt cactcactgt
                                                                      360
tttgcagttt ctccctcagt ccctggttct ttcttctcac ataatcccaa tttcaattta
                                                                      420
tagttcatgg cccaggcaga gtcattcatc acggcatctc ctgagctaaa ccagcacctg
                                                                      480
ctctgctcac ttcttgactg gctgctcatc atcagccctc ttgcagagat ttcatttcct
                                                                      540
cccgtgccag gtacttcacg caccaagctc a
                                                                      571
                      <210> 49
      <211> 511
      <212> DNA
      <213> Homo sapien
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                                                                       60
caacaaatat ccccaaaata aagcaagcat atatatcttg aatgtgtaat aatccagtga
                                                                      120
taaacaagag cagtacttta aaagaaaaaa aaatatgtat ttctgtcagg ttaaaatgag
                                                                      180
aatcaaaacc atttactctg ctaactcatt attttttgct ttctttttgg ttaagagagg
                                                                      240
caatgcaata cactgaaaaa ggtttttatc ttatctggca ttggaattag acatattcaa
                                                                      300
accccagccc ccatttccaa actttaagac cacaaacaag taatttactt ttctgaacat
                                                                      360
tggttttttc tggaaaatgg gaattataaa atagactttg cagactctta tgagattaaa
                                                                      420
taagataatg tatgaaattc tttcttcttt tttacttctt tttccttttt gagatggagt
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ctcacccgt cacccagget ggagtacagt g
                                                                      511
      <210> 50
      <211> 561
      <212> DNA
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<213> Homo sapien

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                                                                        60
                                                                       120
tcaacagatt gttgatcacc taccatatgc ttggtattgt tctaattgct ggggatacag
                                                                       180
caagaggttc tgcagaactt catggagcat gaaagtaaat aaacaaagtt aatttcaagg
                                                                       240
ccaggcatgg ttgctcacac ctttagtccc agcactttgg gaggctgagg caggtggatc
                                                                       300
acttgggccc aggagttcaa ggctgcagtg agccaagatt gtgccactac tctccaggct
                                                                       360
gggcaacaga gcaagaccct gtctcagggg gaacaaaaag ttaatttcag attttgttaa
                                                                       420
gtgctgtaaa ggaagtaaat aggttgatat tcaagagagc acctgaaggc caggcgtggt
                                                                       480
ggctcacgcc tgtggtctaa cgctttggga agcccgagcg ggcggatcac aaggtcagga
                                                                       540
gaattttggc caggcatggt g
                                                                       561
      <210> 51
      <211> 451
      <212> DNA
      <213> Homo sapien
      <400> 51
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atacagggat tacgcctgtg tatgccgaca cttaaatact gtaccaggac cactgctgtg
                                                                       120
cttaggtctg tattcagtca ttcagcatgt agatactaaa aatatactgt agtgttcctt
                                                                       180
taaggaagac tgtacagggt gtgttgcaag atgacattca ccaatttgtg aattatttca
                                                                       240
acccagaaga tacctttcac tctataaact tgtcataggc aaacatgtgg tgttagcatt
                                                                       300
gagagatgca cacaaaaatg ttacataaaa gttcagacat tctaatgata agtgaactga
                                                                       360
aaaaaaaaa aaccccacat ctcaattttt gtaacaagat aaagaaaata atttaaaaac
                                                                       420
acaaaaaatg gcattcagtg ggtacaaagc c
                                                                       451
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      <211> 682
      <212> DNA
      <213> Homo sapien
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aaacgtgaag attaacttaa ttgtcaaata ttcctcattg ccccaaatca gtatttttt
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tatttctatg caaaagtatg ccttcaaact gcttaaatga tatatgatat gatacacaaa
                                                                      180
ccagttttca aatagtaaag ccagtcatct tgcaattgta agaaataggt aaaagattat
                                                                      240
aagacacctt acacacaca acacacaca acacacacgt gtgcaccgcc aatgacaaaa
                                                                      300
aacaatttgg cctctcctaa aataagaaca tgaagaccct taattgctgc caggagggaa
                                                                      360
cactgtgtca cccctcccta caatccaggt agtttccttt aatccaatag caaatctggg
                                                                      420
catatttgag aggagtgatt ctgacagcca csgttgaaat cctgtgggga accattcatg
                                                                      480
tecacecact ggtgeeetga aaaaatgeea ataattttte geteeeactt etgetgetgt
                                                                      540
ctcttccaca tcctcacata gaccccagac ccgctggccc ctggctgggc atcgcattgc
                                                                      600
tggtagagca agtcataggt ctcgtctttg acgtcacaga agcgatacac caaattgcct
                                                                      660
ggtcggtcat tgtcataacc ag
                                                                      682
      <210> 53
      <211> 311
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
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<222> (1)...(311).
      <223> n = A, T, C or G
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tatatettte attatgeeat ettatettet aatgbeaagg gaacagwtge taametgget
                                                                       120
tctgcattwa tcacattaaa aatggctttc ttggaaaatc ttcttgatat gaataaagga
                                                                       180
tettttavag ccatcattta aagemggntt etetecaaca egagtetget sasggggggk
                                                                       240
gagetgtgaa etetggetga aggettteee atacacactg caatgaemtg gtttetgaee
                                                                       300
agbgtgagtt a
                                                                       311
      <210> 54
      <211> 561
      <212> DNA
                                                               ....
      <213> Homo sapien
      <400> 54
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cctccatcat cgggttcata ctggagagaa accctatgta tgtaatgaat gcggcagagc
                                                                       120
ctttggtttt aactctcatc ttactgaaca cgtaaggatt cacacaggag aaaaacccta
                                                                       180
tqtt:qtaat gagtgcggca aagcctttcg tcggagttcc actcttgttc agcatcgaag
                                                                       240
agttcacact ggggagaagc cctaccagtg cgttgaatgt gggaaagctt tcagccagag
                                                                       300
ctcccagctc accetacatc agccgagttc acactggaga gaagccctat gactgtqqtq
                                                                       360
actgtgggaa ggccttcagc cggaggtcaa ccctcattca gcatcagaaa gttcacagcg
                                                                       420
gagagactcg taagtgcaga aaacatggtc cagcctttgt tcatggctcc agcctcacag
                                                                       480
cagatggaca gattcccact ggagagaagc acggcagaac ctttaaccat ggtgcaaatc
                                                                       540
tcattctgcg ctggacagtt c
                                                                       561
      <210> 55
      <211> 811
      <212> DNA
      <213> Homo sapien
      <400> 55
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actgcagece tgacetectg gactcaaaca attetectge etcagecetg caagtagerg
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ggactgtggg tgcatgccac catgcctggc taacttttgt agtttttgta aagatggggt
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tttgccatgt tgcacatgct ggtcttgaac tcctgagctc aaacgatctg cccacctcgg
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cctcccagaa tgttgggatt acaggggtaa accaccacgc ctggccccat tagggtattc
                                                                      300
ttagcatcca cttgctcact gagattaatc ataagagatg ataagcactg gaagaaaaa
                                                                      360
atttttacta ggctttggat attttttcc tttttcagct ttatacagag gattggatct
                                                                      420
ttagttttcc tttaactgat aataaaacat tgaaaggaaa taagtttacc tgagattcac
                                                                      480
agagataacc ggcatcactc ccttgctcaa ttccagtctt taccacatca attattttca
                                                                      540
gaggtgcagg ataaaggcct ttagtctgct ttcgcacttt ttcttccact tttttgtaaa
                                                                      600
cctgttgcct gacaaatgga attgacagcg tatgccatga ctattccatt tgtcaggcat
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acgctgtcaa tttttccacc aatcccttgt ctctctttgg agagatcttc ttatcagcta
                                                                      720
gtcctttggc aaaagtaatt gcaacttctt ctaggtattc tattgtccgt tccactggtg
                                                                      780
gaaccctgg gaccaggact aaaacctcca g
                                                                      811
      <210> 56
      <211> 591
      <212> DNA
      <213> Homo sapien
      <220>
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```
<221> misc_feature
       <222> (1)...(591)
       <223> n = A, T, C or G
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                                                                        120
acaaaactag ggggctctgt cttctcatac atcatacaat tttcaagtat ttttttatg
                                                                        180
tacaaagagc tactctatct gaaaaaaaat taaaaaaataa atgagacaag atagtttatg
                                                                        240
catcctagga agaaagaatg ggaagaaaga acggggcagt tgggtacaga ttcctgtccc
                                                                        300
ctgttcccag ggaccactac cttcctgcca ctgagttccc ccacagcctc acccatcatg
                                                                        360
tcacagggca agtgccaggg taggtgggga ccagtggaga caggaaccag caacatactt
                                                                        420
tggcctggaa gataaggaga aagtctcaga aacacactgg tgggaagcaa tcccacnggc
                                                                       480
cgtgccccan gagcttccca cctgctgctg gctccctggg tggctttggg aacagcttgg
                                                                       540
gcaggccctt ttgggtgggg nccaactggg cctttgggcc cgtgtggaaa g
                                                                       591
      <210> 57
      <211> 481
      <212> DNA
      <213> Homo sapien
      <400> 57
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aattatgatt tatagccttc tcaaatacct gccatacttg atatctcaac cagagctaat
                                                                       120
tttacctctt tacaaattaa ataagcaagt aactggatcc acaatttata atacctgtca
                                                                       180
attttttctg tattaaacct ctatcatagt ttaagcctat tagggtactt aatccttaca
                                                                       240
aataaacagg tttaaaatca cctcaatagg caactgccct tctggttttc ttctttgact
                                                                       300
aaacaatctg aatgcttaag attttccact ttgggtgcta gcagtacaca gtgttacact
                                                                       360
ctgtattcca gacttcttaa attatagaaa aaggaatgta cactttttgt attcttctg
                                                                       420
agcagggccg ggaggcaaca tcatctacca tggtagggac ttgtatgcat ggactacttt
                                                                       480
а
                                                                       481
      <210> 58
      <211> 141
      <212> DNA
      <213> Homo sapien
      <400> 58
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                                                                        60
acaggwtcat gccattctcc tgcctcagca tctggagtag ctgggactac aggcgccagc
                                                                       120
caccatgccc agctaatttt t
                                                                       141
      <210> 59
      <211> 191
      <212> DNA
      <213> Homo sapien
      <400> 59
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                                                                        60
acaagacttg ggagtgattc acacctggaa caacatactg gacttcacac tggabagaaa
                                                                       120
ccttacaagt gtaatgagtg tggcaaagcc tttggcaagc agtcaacact tattcaccat
                                                                       180
caggcaattc a
                                                                       191
      <210> 60
      <211> 480
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<212> DNA
      <213> Homo sapien
      <400> 60
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                                                                        60
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                                                                       120
aggitacata acaggitgate aagecegtae tittiteeta cagicaggie igeeggeeee
                                                                       180
ggttttagct gaaatatggg ccttatcaga tctgaacaag gatgggaaga tggaccagca
                                                                       240
agagttetet atagetatga aacteateaa gttaaagttg cagggeeaac agetgeetgt
                                                                       300
agtecteect cetateatga aacaaceece tatgttetet ceactaatet etgetegttt
                                                                       360
tqqqatqqqa agcatqccca atctqtccat tcatcagcca ttqcctccag ttqcacctat
                                                                       420
agcaacaccc ttgtcttctg ctacttcagg gaccagtatt cctccctaat gatgcctgct
                                                                       480
      <210> 61
      <211> 381
      <212> DNA
      <213> Homo sapien
      <400> 61
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                                                                        60
tgtgtattat agctttctct gagttccttc agctgattgt taaatgaatc catttctgag
                                                                       120
agcttagatg cagtttcttt ttcaagagca tctaattgtt ctttaagtct ttggcataat
                                                                       180
tetteettt etgatgaett tetatgaagt aaactgatee etgaateagg tgtgttaetg
                                                                       240
agctgcatgt ttttaattct ttcgtttaat agctgcttct cagggaccag atagataagc
                                                                       300
ttattttgat attccttaag ctcttggtga agttgttcga tttccataat ttccaggtca
                                                                       360
cactggttat cccaaacttc t
                                                                       381
      <210> 62
      <211> 906
      <212> DNA
      <213> Homo sapien
      <400> 62
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tgaggcacct aggccgcggc accccggcga caggaagccg tcctgaaccg ggctaccqgg
                                                                       120
taggggaagg gcccgcgtag tcctcgcagg gccccagagc tqqaqtcqqc tccacaqccc
                                                                       180
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qaqqaactct catttcttcc ctcqctcctt cacccccac ctcatqtaqa aaqqtqctqa
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gcgctttggt gggcgtggag ttggggttgg gggggtgggt gggggttctt ttttggagtg
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ctggggaact tttttccctt cttcaggtca ggggaaaggg aatgcccaat tcagagagac
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gcggcaqctc taacagcaga gagcgtcacc gcttggtatc qaaqcacaaq cqqcataaqt
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ccaaacactc caaagacatg gggttggtga cccccgaagc agcatccctg ggcacagtta
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tcaaaccttt ggtggagtat gatgatatca gctctgattc cgacaccttc tccgatgaca
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tggccttcaa actagaccga agggagaacg acgaacgtcg tggatcagat cggagcgacc
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 tcaggettgg ggtaccaaac tcatgetetg tactgttttg geeccatgeg gtgagaggaa
 aacctagaaa aagattggtc gtgctaagga atcagctgcc ccctcatcct ccgcatccaa
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                                                                     300
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agtggcctct ggaggctcgt ggcctaaggc agggctccgt aaggctgatc ggctgaactg
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gctgcagcca ggggccagag tcagttcagg gagtggtcct cggccctcaa agctcctccg
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aggtgcctgg ctgctccagg cctctaggct gggctgatgg gtttctccag gacacaagta
                                                                     300
tcattaaagc caccctctcc tcagcttgtc aggccgcaca tgtgggacag gctgtgctca
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caacccctc gcctgccctg ccctccatca ggaggagcca gtggaacctt cggaaagctc
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ccagcatete agcagecete aaaagtegte etggggeaag etetggttet eetgactgga
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                                                                     511
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gottaactga aatagogtoo atooaaaagt gggtttaagg taaaactaco tgacgatatt
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ggcggggatc ctgcagtttg gactgcttgc cgggtttgtc cagggttccg ggtctgttct
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tggcactcat ggggacaggc atcctgctcg tctgtggggc cccgctggag cccttacgtg
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aagctgaagg tatcgaccst agggggctct agggcagtgg gaccttcatc cggaactaac
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atttttccat gaagatgtac ggaaatctga tgttgaatat gaaaatggcc cccaaatgga
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attccaaaag gttaccacag gggctgtaag acctagtgac cctcctaagt gggaaagagg
                                                                    240
aatggagaat agtatttctg atgcatcaag aacatcagaa tataaaactg agatcataat
                                                                    300
gaaggaaaat tocatatoca atatgagttt actoagagac agtagaaact attoccagg
                                                                    359
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      <211> 450
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```
<212> DNA
      <213> Homo sapien
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      <223> n = A,T,C or G
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agtggaggag gacacaggac tagcccacca ccttctcttc ccggtctccc aagatgactg
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cttatagagt ggaggaggca aacaggtccc ctcaatgtac cagatggtca cctatagcac
                                                                      240
cagetecaga tggccaegtg gttgcagetg gaeteaatga aactetgtga caaccagaag
                                                                      300
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                                                                      420
actgnctttt ggatgctctc ttgggccacg
                                                                       450
      <210> 68
      <211> 511
      <212> DNA
      <213> Homo sapien
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cacagcagaa acgccagcag agaaaatggg agccgagagt ccttagccct ggagctgagg
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ctgcctctgg gctgacccgc tggctgtacg tggccagaac tggggttggc atctggcatc
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catttgaggc cagggtggag gaaagggagg ccaacagagg aaaacctatt cctqctqtqa
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caacacagcc cttgtcccac gcagcctaag tgcagggagc gtgatgaagt caggcagcca
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gtcggggagg acgaggtaac tcagcagcaa tgtcaccttg tagcctatgc gctcaatggc
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ccggaggggc agcaacccc cgcacacgtc agccaacagc agtgcctctg caggcaccaa
                                                                       480
gagagcgatg atggacttga gcgccgtgtt c
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                                                                      120
gaggttaggg cccccaggcg ggctaagtgc tattggcctg ctcctgctca aagagagcca
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tagccagctg ggcacggccc cctagcccct ccaggttgct gaggcggcag cggtggtaga
                                                                      240
gttcttcact gagccgtggg ctgcagtctc gcagggagaa cttctgcacc agccctggct
                                                                       300
ctacggcccg aaagaggtgg agccctgaga accggaggaa aacatccatc acctccagcc
                                                                       360
cctccagggc ttcctcctct tcctggcctg ccagttcacc tgccagccgg gctcgggccg
                                                                       420
ccaggtagtc agcgttgtag aagcagccct ccgcagaagc ctgccggtca aatctccccg
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      <212> DNA
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  acttttacct gtgcaaaaag cacattttcc acctccttct catggcattt gtgtaaggtg
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  gattagcaag ggacccctca ctaagtgttg atggagttag gacagagctc agctgtttga
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  atctcagage ccaggeaget ggagetgggt aggatectgg agetggeact aatgtgaggt
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  gcattccctc caacccaggc tcagatccgg aacctgaccg tgctgacccc cgaaggggag
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  gcagggctga gctggcccgt tgggctccct gctcctttca caccacactc tcgctttgag
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  gtgctgggct gggactactt cacagagcag c
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                                                                       420
                                                                       480
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                                                                       240
taaagttgca gggccaacag ctgcctgtag tectecetee tatcatgaaa caaceeecta
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                                                                       720
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acctcactga catggccaaa gctggacagc cactaccact gacgttgcct cccgagcttg
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gaaagaaaag totocacotg gaactggaag cagtgaatgg aaaacatcag cagatotcag
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gcagactaca agatgtccaa atcagaaagc aaacacaaaa gactgagcta gaagttttgg
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ataaacagtg tgacctggaa attatggaaa tcaaacaact tcaacaagag cttaaggaat
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atcaaaataa gcttatctat ctggtccctg agaagcagct attaaacgaa agaattaaaa
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acatgcaget cagtaacaca cetgatteag ggateagttt actteataaa aagteateag
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aaaaggaaga attatgccaa agacttaaag aacaattaga tgctcttgaa aaagaaactg
                                                                      1860
catctaagct ctcagaaatg gattcattta acaatcagct gaaggaactc agagaaagct
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ataatacaca gcagttagcc cttgaacaac ttcataaaat caaacgtgac aaattgaagg
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taatcagtat ctcagagggc tctaaggtgc caagaagtct cactggacat ttaagtgcca
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acaaaggcat actttcggaa tcgccaagtc aaaactttct aacttctgtc tctctcagag
                                                                      240
acaagtgaga ctcaagagtc tactgcttta gtggcaacta cagaaaactg gtgttaccca
                                                                       300
gaaaaacagg agcaattaga aatggttcca atatttcaaa gctccgcaaa caggatgtgc
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      <210> 74
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attcatgtga actagacaag tgtgttaaga gtgataagta aaatgcacgt ggagacaagt
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gcatccccag atctcaggga cctcccctg cctgtcacct ggggagtgag aggacaggat
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agtgcatgtt ctttgtctct gaatttttag ttatatgtgc tgtaatgttg ctctgaggaa
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gcccctggaa agtctatccc aacatatcca catcttatat tccacaaatt aagctgtagt
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agtaatgggt caaatgattc actttttatg atgcttccaa aggtgccttg gcttctcttc
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ccaactgaca aatgccaaag ttgagaaaaa tgatcataat tttagcataa acagagcagt
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cggcgacacc gattttataa ataaactgag caccttcttt ttaaacaaac aaatgcgggt
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gagccagaac tctatcgggc accaggataa catctctcag tgaacagagt tgacaaggcc
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cattctaccc tgcaagccaa gttctgtaag agaaatgcct gagttctagc tcaggttttc
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atatacette catgaageae acacagaett ttgaaageaa ggacaatgae tgettgaatt
 gaggccttga ggaatgaagc tttgaaggaa aagaatactt tgtttccagc cccttccca
                                                                       1380
 cactetteat gtgttaacca etgeetteet ggaeettgga geeaeggtga etgtattaca
                                                                       1440
 tgttgttata gaaaactgat tttagagttc tgatcgttca agagaatgat taaatataca
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                                                                       1560
 tttccta
                                                                       1567
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       <212> DNA
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                                                                         60
 ggaagacctg ggggaaaaca ccatggtttt atccaccctg agatctttga acaacttcat
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 ctctcagcgt gcggagggag gctctggact ggatatttct acctcggccg cgaccacgct
                                                                        180
                                                                        240
       <210> 76
       <211> 330
       <212> DNA
       <213> Homo sapien
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       <221> misc_feature
       <222> (1)...(330)
       <223> n = A, T, C \text{ or } G
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ggtgggtgca gatggcatcc actccggtgg cttccccatc tttctctggc ctgagcaagg
                                                                        60
teageetgea gecagagtae agagggeeaa caetggtgtt ettgaacaag ggeettagea
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ggccctgaag grccctctct gtagtgttga acttcctgga gccaggccac atgttctcct
                                                                       180
cataccgcag gytagygatg gtgaagttga gggtgaaata gtattmangr agatggctgg
                                                                       240
                                                                       300
caracetyce egggeggeeg etesaaatee
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      <211> 361
      <212> DNA
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                                                                        60
cagecaccag agtggatget gtetgeacce ategteetga ecceaaaage eetggactgg
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acagagageg getgtactgg aagetgagee agetgaceea eggeateaet gagetgggee
                                                                      180
cctacaccct ggacagggac agtctctatg tcaatggttt cacccatcgg agctctgtac
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ccaccaccag caccggggtg gtcagcgagg agccattcaa cctgcccggg cggccgctcg
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                                                                      360
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      <210> 78
      <211> 356
      <212> DNA
      <213> Homo sapien
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<221> misc_feature
      <222> (1)...(356)
      <223> n = A, T, C or G
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gaagttcaac accacggaga gggtccttca gggcctgctc aggtccctgt tcaagagcac
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cagtgttggc cctctgtact ctggctgcag actgactttg ctcagacttg agaaacatgg
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                                                                      356
      <210> 79
      <211> 226
      <212> DNA
      <213> Homo sapien
      <400> 79
agegtggteg eggeegaggt ceagtegeag catgetettt etectgeeca etggeacagt
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gaggaagatc tctgctgtca gtgagaaggc tgtcatccac tgagatggca gtcaaaagtg
                                                                      120
catttaatac acctaacgta tcgaacatca tagcttggcc caggttatct catatgtgct
                                                                      180
cagaacactt acaatagcct gcagacctgc ccgggcggcc gctcga
                                                                      226
      <210> 80
      <213> Homo sapien - ·
      <220>
      <221> misc_feature
      <222> (1)...(444)
      <223> n = A, T, C or G
      <400> 80
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gsmgmssgag gmwggwgtyy cwgaggttcy rarrtccact gtggaggtcc caggagtgct
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ggtgtagggg cccagctctt yratgycatt ggycagttkg ctyagctccc agtacagccr
                                                                      300
ctctckgyyg mgwccagsgc ttttggggtc aagatgatgg atgcagatgg catccactcc
                                                                      360
agtggctgct ccatccttct cggacctgag agaggtcagt ctgcagccag agtacagagg
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      <210> 81
      <211> 310
      <212> DNA
      <213> Homo sapien
      <400> 81
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                                                                      120
gatcagtcag actggctgtt ctcagttctc acctgagcaa ggtcagtctg cagccagagt
                                                                      180
acagagggcc aacactggtg ttcttgaaca agggcttgag cagaccctgc agaaccctct
                                                                      240
tccgtggtgt tgaacttcct ggaaaccagg gtgttgcatg tttttcctca taatgcaagg
                                                                      300
ttggtgatgg
                                                                      310
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<210> 82
       <211> 571
       <212> DNA
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       <220>
       <221> misc feature
       <222> (1)...(571)
       <223> n = A, T, C or G
       <400> 82
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 tacaaatgga atttcatctt gtttccatgc tgagtagtga aacagtgaca aagctaatca
                                                                        60
 taataaccta catcaaaaga gaactaagct aacactgctc actttctttt taacaggcaa
                                                                        120
 aatataaata tatgcactct anaatgcaca atggtttagt cactaaaaaa ttcaaatggg
                                                                       180
 atcttgaaga atgtatgcaa atccagggtg cagtgaagat gagctgagat gctgtgcaac
                                                                       240
 tgtttaaggg ttcctggcac tgcatctctt ggccactagc tgaatcttga catggaaggt
                                                                       300
 tttagctaat gccaagtgga gatgcagaaa atgctaagtt gacttagggg ctgtgcacag
                                                                       360
 gaactaaaag gcaggaaagt actaaatatt gctgagagca tccaccccag gaaggacttt
                                                                       420
 accttccagg agctccaaac tggcaccacc cccagtgctc acatggctga ctttatcctc
                                                                       480
                                                                       540
 cgtgttccat ttggcacagc aagtggcagt g
                                                                       571
       <210> 83
       <211> 551
       <212> DNA
      <213> Homo sapien
      <400> 83
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                                                                        60
aagggaaaag atgcttctgg gaacaaggtt aaagccgagc cagccaaaat agaagctttc
                                                                       120
cgagetteae tttccaaget aggggatgte tatgtcaatg atgettttgg cactgeteae
                                                                       180
agageceaea getecatggt aggagteaat etgecaeaga aggetggtgg gtttttgatg
                                                                       240
aagaaggage tgaactactt tgcaaaggee ttggagagee cagagegace ettectggee
                                                                       300
atcctgggcg gagctaaagt tgcagacaag atccagctca tcaataatat gctggacaaa
gtcaatgaga tgattattgg tggtggaatg gcttttacct tccttaaggt gctcaacaac
                                                                       360
atggagattg gcacttctct gtttgatgaa gagggagcca agattgtcaa agacctaatg
                                                                       420
                                                                       480
tccaaagctg agaagaatgg tgtgaagatt accttgcctg ttgactttgt cactgctgac
                                                                       540
aagtttgatg a
                                                                       551
      <210> 84
      <211> 571
      <212> DNA
      <213> Homo sapien
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taagttetga ttecaactta getaatteat tetgagaact gtggtatagg tggegtgtet
                                                                       60
                                                                      120
cttctagctg ggacaaaagt tctttgtttt ccccctgtag agtatcacag accttctgct
                                                                      180
gaagctggac ctctgtctgg gccttggact cccaaatctg cttgtcatgt tcaagcctgg
                                                                      240
aaatgttaat ctttaattct tccatatgga tggacatctg tctaagttga tcctttagaa
                                                                      300
cactgcaatt atcttctttg agtctaattt cttcttcttt gctttgaatc gcatcactaa
acttectete ceatttetta getteateta teaceetgte acgateatee tggagggaag
                                                                      360
acatgetett agtaaagget geaagetggg teacagtact gtecaagttt teetgaagtt
                                                                      420
                                                                      480
gctgaacttc cttgtctttc ttgttcaaag taacctgaat ctctccaatt gtctcttcca
                                                                      540
```

```
agtggacttt ttctctgcgc aaagcatcca q
                                                                       571
      <210> 85
      <211> 561
      <212> DNA
      <213> Homo sapien
      <400> 85
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aatcaaagga ttcagcatgt ggtggaagct gtgaggcaag agaaacaaga actgtatggc
                                                                      120
aagttaagaa gcacagaggc aaacaagaag gagacagaaa agcagttgca ggaagctgag
                                                                      180
caagaaatgg aggaaatgaa agaaaagatg agaaagtttg ctaaatctaa acagcagaaa
                                                                      240
atcctagagc tggaagaaga gaatgaccgg cttagggcag aggtgcaccc tgcaggagat
                                                                      300
acagetaaag agtgtatgga aacaettett tettecaatg ceageatgaa ggaagaaett
                                                                      360
qaaaqggtca aaatggagta tgaaaccctt tctaagaagt ttcagtcttt aatgtctgag
                                                                      420
aaagactctc taagtgaaga ggttcaagat ttaaagcatc agatagaagg taatgtatct
                                                                       480
aaacaagcta acctagaggc caccgagaaa catgataacc aaacgaatgt cactgaagag
                                                                      540
ggaacacagt ctataccagg t
                                                                       561
      <210> 86
      <211> 795
      <212> DNA
      <213> Homo sapien
      <400> 86
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aattctcacc gttacaacaa ccccatgagg tatttattcc cattctatag atagggaaac
                                                                      120
cacageteaa gtaagttagg aaactgagee aagtatacae agaataegaa gtggeaaaae
                                                                      180
tagaaggaaa gactgacact gctatctgct ggcctccagt gtcctggctc ttttcacacg
                                                                      240
ggttcaatgt ctccagcgct gctgctgctg ctgcattacc atgccctcat tgtttttctt
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cctctggtgt tcaactgcat ccttcaaaga atctaactca ttccagagac cacttatttc
                                                                      360
tttctctctt tctgaaatta cttttaataa ttcttcatga gggggaaaag aagatgcctg
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ttggtagttt tgttgtttaa gctgctcaat ttgggactta aacaatttgt tttcatcttg
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tacatcctgt aacagctgtg ttttgctaga aagatcactc tccctcttt ttagcatggc
                                                                      540
ttctaacctc ttcaattcat tttccttttc tttcaacaca atctcaagtt cttcaaactg
                                                                      600
tgatgcagaa gaggcctctt tcaagttatg ttgtgctact tcctgaacat gtgcttttaa
                                                                      660
agattcattt tcttcttgaa gatcctgtaa ccacttccct gtattggcta ggtctttctc
                                                                      720
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                                                                      780
caggagette agaac
                                                                      795
      <210> 87
      <211> 594
      <212> DNA .
      <213> Homo sapien
      <400> 87
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caactgggtt tatgtcttca tattttatat ttttgtaaat taaaaaaatt acaagtttta
                                                                      120
aatagccaat ggctggttat attttcagaa aacatgatta gactaattca ttaatggtgg
                                                                      180
cttcaagctt ttccttattg gctccagaaa attcacccac cttttgtccc ttcttaaaaa
                                                                      240
actggaatgt tggcatgcat ttgacttcac actctgaagc aacatcctga cagtcatcca
                                                                      300
catctacttc aaggaatatc acgttggaat acttttcaga gagggaatga aagaaaggct
                                                                      360
tgatcatttt gcaaggccca caccacgtgg ctgagaagtc aactactaca agtttatcac
                                                                      420
ctgcagcgtc caaggcttcc tgaaaagcag tcttgctctc gatctgcttc accatcttgg
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ctgctggagt ctgacgagcg gctgtaagga ccgatggaaa tggatccaaa qcaccaaaca
                                                                      540
```

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gagetteaag actegetget tggettgaat teggateega tategeeatg geet
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        <210> 88
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        <213> Homo sapien
        <400> 88
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  tttatatttt tgtaaattaa aaaaattmca agttttaaat agccaatggc tggttatatt
                                                                         .60
 ttcagaaaac atgattagac taattcatta atggtggctt caagcttttc cttattggct
                                                                         120
 ccagaaaatt cacccacctt ttgtcccttc ttaaaaaaact ggaatgttgg catgcatttg
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 acttcacact ctgaagcaac atcctgacag tcatccacat ctacttcaag gaatatcacg
                                                                        240
 ttggaatact tttcagagag ggaatgaaag aaaggcttga tcattttgca aggcccacac
                                                                        300
 cacgtggctg agaagtcaac tactacaagt ttatcacctg cagcgtccaa ggcttcctga
                                                                        360
 aaagcagtct tgctctcgat ctgcttcacc atcttggctg ctggagtctg acgagcggct
                                                                        420
 gtaaggaccg atggaaatgg atccaaagca ccaaacagag cttcaagact cgctgcttgg
                                                                        480
                                                                        540
 catgaattcg gatccga
                                                                        557
       <210> 89
       <211> 561
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1) ... (561)
       <223> n = A, T, C \text{ or } G
       <400> 89
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gcacctggcc acagggtcca ctgaaacggg gaggggatgg cagcttgtaa tgtggctttt
                                                                        60
gccacaaccc ccttctgaca gggaaggcct tagattgagg ccccacctcc catggtgatg
                                                                        120
gggagctcag aatggggtcc agggagaatt tggttagggg gaggtgctag ggaggcatga
                                                                       180
gcagagggca ccctccgagt ggggtcccga gggctgcaga gtcttcagta ctgtccctca
                                                                       240
cagcagctgt ctcaaggctg ggtccctcaa aggggcgtcc cagcgcgggg cctccctgcg
                                                                       300
caaacacttg gtacccctgg ctgcgcagcg gaagccagca ggacagcagt ggcgccgatc
                                                                       360
agcacaacag acgccctggc ggtagggaca gcaggcccag ccctgtcggt tgtctcggca
                                                                       420
gcaggtctgg ttatcatggc agaagtgtcc ttcccacact tcacgtcctt cacacccacg
                                                                       480
                                                                       540
tganggctac nggccaggaa g
                                                                       561
      <210> 90
      <211> 561
      <212> DNA
      <213> Homo sapien
      <400> 90
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actgcagtgg aagccccgtg ggcagcagtg atggccatcc ccgcatgcca cggcctctgg
                                                                        60
gaaggggcag caactggaag teeetgagae ggtaaagatg caggagtgge eggeagagea
                                                                       120
gtgggcatca acctggcagg ggccacccag atgcctgctc agtgttgtgg gccatttgtc
                                                                       180
cagaagggga cggcagcagc tgtagctggc tectecgggg tecaggeagc aggccacagg
                                                                       240
gcagaactga ccatctgggc accgcgttcc agccaccagc cctgctgtta aggccaccca
                                                                       300
geteaceagg gtecacatgg tetgeetgeg teegacteeg eggteettgg geeetgatgg
                                                                       360
ttctacctgc tgtgagctgc ccagtgggaa gtatggctgc tgccaatgcc caacgccacc
                                                                       420
                                                                       480
```

```
tgctgctccg atcacctgca ctgctgcccc aagacactgt gtgtgacctg atccagagta
                                                                     540
agtgcctctc caaggagaac g
                                                                     561
      <210> 91
      <211> 541
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(541)
      <223> n = A, T, C or G
      <400> 91
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gtctccctgg gctctgtttg gctctcggta aggcaggcct acaccttttc ctctcctcta
                                                                     120
tggagagggg aatatgcatt aaggtgaaaa gtcaccttcc aaaagtgaga aagggattcg
                                                                     180
attgctgctt caggactgtg gaattatttg gaatgtttta caaatggttg ctacaaaaca
                                                                     240
acaaaaaagg taattacaaa atgtgtacat cacaacatgc tttttaaaga cattatgcat
                                                                     300
tgtgctcaca ttcccttaaa tgttgtttcc aaaggtgctc agcctctagc ccagctggat
                                                                     360
tctccgggaa gaggcagaga cagtttggcg aaaaagacac agggaaggag ggggtggtga
                                                                     420
aaggagaaag cagcetteca gttaaagate ageeeteagt taaaggteag etteeegean
                                                                     480
gctggcctca ngcggagtct gggtcagagg gaggagcagc agcagggtgg gactggggcg
                                                                     540
                                                                     541
      <210> 92
      <211> 551
      <212> DNA
      <213> Homo sapien
      <400> 92
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gtgaagcgca agatccaggt tctgcagcag caggcagatg atgcagagga gcgagctgag
                                                                     120
cgcctccagc gagaagttga gggagaaagg cgggcccggg aacaggctga ggctgaggtg
                                                                     180
gcctccttga accgtaggat ccagctggtt gaagaagagc tggaccgtgc tcaggagcgc
                                                                     240
ctggccactg ccctgcaaaa gctggaagaa gctgaaaaag ctgctgatga gagtgagaga
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ggtatgaagg ttattgaaaa ccgggcctta aaagatgaag aaaagatgga actccaggaa
                                                                     360
atccaactca aagaagctaa gcacattgca gaagaggcag ataggaagta tgaagaggtg
                                                                     420
480
gcagagtece gttgccgaga gatggatgag cagattagae tgatggacca gaacetgaag
                                                                     540
tgtctgagtg c
                                                                     551
      <210> 93
      <211> 531
      <212> DNA
      <213> Homo sapien
      <400> 93
gagaacttgg cetttattgt gggcccagga gggcacaaag gtcaggaggc ccaagggagg
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gatctggttt tctggatagc caggtcatag catgggtatc agtaggaatc cgctgtagct
                                                                     120
gcacaggeet cacttgetge agtteegggg agaacacetg cactgeatgg egttgatgae
                                                                     180
ctcgtggtac acgacagagc cattggtgca gtgcaagggc acgcgcatgg gctccgtcct
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cgagggcagg cagcaggagc attgctcctg cacatcctcg atgtcaatgg agtacacagc
                                                                     300
tttgctggca cactttccct ggcagtaatg aatgtccact tcctcttggg acttacaatc
                                                                     360
tcccactttg atgtactgca ccttggctgt gatgtctttg caatcaggct cctcacatgt
                                                                     420
```

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gtcacagcag gtgcctggaa ttttcacgat tttgcctcct tcagccagac acttgtgttc
 atcaaatggt gggcagcccg tgaccctctt ctcccagatg tactctcctc t
                                                                        480
                                                                        531
       <210> 94
       <211> 531
       <212> DNA
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       <220>
       <221> misc_feature
       <222> (1)...(531)
       <223> n = A, T, C or G
       <400> 94
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 ctgcagagtc atcgtgtcaa ttgtgaccat ggaccccggc cttcatgtgc caacagccag
                                                                         60
 teteetgtte gggtggagga gacgtgtgge tgeegetgga cetgeeettg tgtgtgeaeg
                                                                        120
                                                                        180
 ggcagttcca ctcggcacat cgtcaccttc gatgggcaga atttcaagct tactggtagc
                                                                        240
tgetectatg teatetttea aaacaaggag caggaeetgg aagtgeteet ceacaatggg
                                                                        300
gcctgcagcc ccggggcaaa acaagcctgc atgaagtcca ttgagattaa gcatgctggc
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gtctctgctg agctgcacag taacatggag atggcagtgg atgggagact ggtccttgcc
ccgtacgttg gtgaaaacat ggaagtcagc atctacggcg ctatcatgta tgaagtcagg
                                                                       420
                                                                       480
tttacccatc ttggccacat cctcacatac accgccncaa aacaacgagt t
                                                                       531
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       <211> 605
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       <213> Homo sapien
      <400> 95
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                                                                       120
rsgraraytt agacaycccm cctcwgagac gsagkaccar gtgcagaggt ggactctttc
                                                                       180
tggatgttgt agtcagacag ggtgcgtcca tcttccagct gtttcccagc aaagatcaac
                                                                       240
ctctgctgat caggagggat gccttcctta tcttggatct ttgccttgac attctcgatg
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gtgtcactgg gctccacctc gagggtgatg gtcttaccag tcagggtctt cacgaagaty
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tgcatcccac ctctgagacg gagcaccagg tgcagggtrg actctttctg gatgttgtag
                                                                       420
tcagacaggg tgcgyccatc ttccagctgc tttccsagca aagatcaacc tctgctggtc
                                                                       480
aggaggratg cetteettgt cytggatett tgcyttgaer tteteratgg tgteactegg
                                                                       540
ctccacttcg agagtgatgg tcttaccagt cagggtcttc acgaagatct gcatcccacc
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tctaa
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      <210> 96
      <211> 531
      <212> DNA
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      <400> 96
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gacagaggtc atgattctga gatgattgga gaccttcaag ctcgaattac atctttacaa
                                                                        60
gaggaggtga agcatctcaa acataatctc gaaaaagtgg aaggagaaag aaaagaggct
                                                                       120
caagacatgc ttaatcactc agaaaaggaa aagaataatt tagagataga tttaaactac
                                                                      180
aaacttaaat cattacaaca acggttagaa caagaggtaa atgaacacaa agtaaccaaa
                                                                      240
                                                                      300
gctcgtttaa ctgacaaaca tcaatctatt gaagaggcaa agtctgtggc aatgtgtgag
atggaaaaaa agctgaaaga agaaagagaa gctcgagaga aggctgaaaa tcgggttgtt
                                                                      360
                                                                      420
```

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cagattgaga aacagtgttc catgctagac gttgatctga agcaatctca gcagaaacta
                                                                     480
gaacatttga ctggaaataa agaaaggatg gaggatgaag ttaagaatct a
                                                                     531
      <210> 97
      <211> 1017
      <212> DNA
      <213> Homo sapien .
            : . .
      <220>
      <221> misc feature
      <222> (1)...(1017)
      <223> n = A, T, C or G
      <400> 97
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ccgggccttc agcagccgct cctacacgag tgggcccggt tcccgcatca gctcctcgag
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cttctcccga gtgggcagca gcaactttcg cggtggcctg ggcggcggct atggtgggc
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cagcggcatg ggaggcatca ccgcagttac ggtcaaccag agcctgctga gcccccttgt
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cctggaggtg gaccccaaca tccaggccgt gcgcacccag gagaaggagc agatcaagac
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cctcaacaac aagtttgcct ccttcataga caaggtacgg ttcctggagc agcagaacaa
                                                                     360
gatgctggag accaagtgga gcctcctgca gcagcagaag acggctcgaa gcaacatgga
                                                                     420
caacatgttc gagagetaca teaacareet taggeggeag etggagaete tgggeeagga
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gaagctgaag ctggaggcgg agcttggcaa catgcagggg ctggtggagg acttcaagaa
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caagtatgag gatgagatca ataagcgtac agagatggag aacgaatttg tcctcatcaa
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gaaggatgtg gatgaagctt acatgaacaa ggtagagctg gagtctcgcc tggaagggct
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qaccgacgag atcaacttcc tcaggcagct gtatgaagag gagatccggg agctgcagtc
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ccagateteg gacacatetg tggtgetgte catggacaac ageegeteec tggacatgga
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cagcatcatt gctgaggtca aggcacagta cgaggatatt gccaaccgca gccgggctga
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ggatgacctg cggcgcacaa agactgagat ctctgagatg aacccggaac atcaqcccgg
                                                                     960
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                                                                    1017
     <210> 98
     <211> 561
     <212> DNA
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     <400> 98
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ggcaggggc tacccagggg cttcctatcc tggggcctac cccgggcagg cacccccagg
                                                                     180
ggettateet ggacaggeae etecetgga geacetggag ettateeegg
                                                                     240
agcacetgea cetggagtet acceagggee acceagegge cetggggeet acceatette
                                                                     300
tggacagcca agtgccaccg gagcctaccc tgccactggc ccctatggcg cccctgctgg
                                                                     360
gccactgatt gtgccttata acctgccttt gcctggggga gtggtgcctc gcatgctgat
                                                                     420
aacaattctg ggcacggtga agcccaatgc aaacagaatt gctttagatt tccaaagagg
                                                                     480
gaatgatgtt gccttccact ttaacccacg cttcaatgag aacaacagga gagtcattgg
                                                                     540
ttgcaataca aagctggata a
                                                                     561
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     <211> 636
     <212> DNA
     <213> Homo sapien .
     <400> 99
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 ggaaacttag acacccccc tcragcgmag kaccargtgc araggtggac tctttctgga
                                                                         60
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tccctcagaa tttgtgtttg ctgcctctat cttgtttttt gtttttctt ctgggggggt
                                                                        300
ctagaacagt gcctggcaca tagtaggcgc tcaataaata cttggttgnt gaatgtctcc
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      <212> DNA
      <213> Homo sapien
      <400> 121
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aacccacgcc tgtaaggtcg gtcttcgtcc atctgctttt ttctgaaata cactaagagc
                                                                        60
agccacaaaa ctgtaacctc aaggaaacca taaagcttgg agtgccttaa tttttaacca
                                                                       120
                                                                       180
gtttccaata aaacggttta ctacct
                                                                       206
      <210> 122
      <211> 131
      <212> DNA
      <213> Homo sapien
      <400> 122
ggagatgaag atgaggaagc tgagtcagct acgggcargc gggcagctga agatgatgag
gatgacgatg tcgataccaa gaagcagaag accgacgagg atgactagac agcaaaaaag
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gaaaagttaa a
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     <210> 123
     <211> 231
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<212> DNA
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      <220>
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      <223> n = A, T, C or G
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                                                                        60
cctcagtggc agtakgctaa kgaagatcaa gctacagsac atyatctaat atgaatgtta
                                                                       120
gcaattacat akcargaagc atgtttgctt tccagaagac tatggnacaa tggtcattwg
                                                                       180
ggcccaagag gatatttggc cnggaaagga tcaagataga tnaangtaaa g
                                                                       231
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      <211> 521
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(521)
      <223> n = A, T, C or G
      <400> 124
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                                                                       120
atcttcagca ggcagctccc accaggactt atctcasaaa attgctgacc gcctgggcct
                                                                       180
ggagctaggc aaggtggtga ctaagaaatt cagcaaccag gagacctgtg tggaaattgg
                                                                       240
tgaaagtgta ccgtggagag gatgtctaca ttgttcagag tggntgtggc gaaatcaatg
                                                                       300
acaatttaat ggagcttttg atcatgatta atgcctgcaa gattgcttca gccagccggg
                                                                       360
ttactgcagt catcccatgc ttcccttatg ccccggcagg ataagaaaga tnagagccgg
                                                                       420
gccgccaatc tcagccaagc ttggtgcaaa tatgctatct gtagcagtgc agatcatatt
                                                                       480
atcaccatgg acctacatgc ttctcaaatt canggctttt t
                                                                       521
      <210> 125
      <211> 341
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(341)
      <223> n = A, T, C or G
atgcaaaagg ggacacaggg ggttcaaaaa taaaaatttc tcttccccct ccccaaacct
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gtaccccagc tccccgacca caaccccctt cctccccgg ggaaagcaag aaggagcagg
                                                                       120
tgtggcatct gcagctggga agagagaggc cggggaggtg ccgagctcgg tgctggtctc
                                                                       180
tttccaaata taaatacgtg tgtcagaact ggaaaatcct ccagcaccca ccacccaagc
                                                                       240
actotccgtt ttctgccggt gtttggagag gggcggnggg cagggggcgcc aggcaccggc
                                                                       300
tggctgcggt ctactgcatc cgctgggtgt gcaccccgcg a
                                                                       341
      <210> 126
      <211> 521
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<212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(521)
        <223> n = A, T, C \text{ or } G
        <400> 126
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 caggeccaga gtggcactgg acagaccatg caggtgatge agcagateat cactaacaca
 ggagagatcc agcagatccc ggtgcagctg aatgccggcc agctgcagta tatccgctta
                                                                        120
 gcccagcctg tatcaggcac tcaagttgtg cagggacaga tccagacact tgccaccaat
                                                                        180
 gctcaacaga ttacacagac agaggtccag caaggacagc agcagttcaa gccagttcac
                                                                        240
 aagatggaca gcagctctac cagatccagc aagtcaccat gcctgcgggc cangacctcg
                                                                        300
 ccageccatg ttcatccagt caagccaacc agccettena egggcaggee ecceaggtga
                                                                        360
 ccggcgactg aagggcctga gctggcaagg ccaangacac ccaacacaat ttttgccata
                                                                        420
                                                                        480
 cagececcag geaatgggea cageetttet teecagagga e
                                                                        521
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       <211> 351
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       <213> Homo sapien
       <400> 127
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 aatgcattta aaaaataaaa gggaggtggg cagcaaacac acaaagtcct agttteetgg
                                                                        60
 gtccctggga gaaaagagtg tggcaatgaa tccacccact ctccacaggg aataaatctg
                                                                       120
 totottaaat goaaagaatg tttocatggo ototggatgo aaatacacag agototgggg
                                                                       180
 tcagagcaag ggatggggag aggaccacga gtgaaaaagc agctacacac attcacctaa
                                                                       240
 ttccatctga gggcaagaac aacgtggcaa gtcttggggg tagcagctgt t
                                                                       300
                                                                       351
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       <211> 521
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       <213> Homo sapien
       <400> 128
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agagttaagg gaaggtttcc tttcattcct gttccttctc ttttgctttt gaacagtttt
                                                                        60
taaatatact aatagctaag tcatttgcca gccaggtccc ggtgaacagt agagaacaag
                                                                       120
gagettgeta agaattaatt ttgetgtttt teaceceatt caaacagage tgeeetgtte
                                                                       180
cctgatggag ttccattcct gccagggcac ggctgagtaa cacgaagcca ttcaagaaag
                                                                       240
gegggtgtga aateactgee acceeatgga cagacceete actetteett ettageegea
                                                                       300
gogotactta ataaatatat ttatactttg aaattatgat aaccgatttt toocatgogg
                                                                       360
catectaagg geaettgeea getettatee ggaeagteaa geaetgttgt tggaeaacag
                                                                       420
                                                                       480
ataaaggaaa agaaaaagaa gaaaacaacc gcaacttctg t
                                                                       521
      <210> 129
      <211> 521
      <212> DNA
      <213> Homo sapien
      <400> 129
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                                                                        60
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cagatetagt ggcagagagg aagatgatga ggaacttetg agacgtegge agetteaaga
                                                                       120
agagcaatta atgaagctta actcaggcct gggacagttg atcttgaaag aagagatgga
                                                                       180
gaaagagage egggaaaggt catetetgtt agecagtege taegattete ceateaacte
                                                                       240
agcttcacat attccatcat ctaaaactgc atctctccct ggctatggaa gaaatgggct
                                                                       300
tcaccggcct gtttctaccg acttcgctca gtataacagc tatggggatg tcagcggggg
                                                                       360
agtgcgagat taccagacac ttccagatgg ccacatgcct gcaatgagaa tggaccgagg
                                                                       420
agtgtctatg cccaacatgt tggaaccaaa gatatttcca tatgaaatgc tcatggtgac
                                                                       480
caacagaggg ccgaaaccaa atctcagaga ggtggacaga a
                                                                       521
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      <213> Homo sapien
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ctgcacggag actctggtgt gggtcttgac gaggtggtca gtgaactcct gatagggaga
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cttggtgaat acagtctcct tccagaggtc gggggtcagg tagctgtagg tcttagaaat
                                                                       180
ggcatcaaag gtggccttgg cgaagttgcc cagggtggca qtgcagcccc gqqctqaqqt
                                                                       240
gtagcagtca tcgataccag ccatcatgag
                                                                       270
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      <211> 341
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      <213> Homo sapien
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                                                                       120
ttatgtataa tagctcatgc atgtgtccat gtcataactg tcttcatacg cttctgcact
                                                                       180
ctggggaaga aggagtacat tgaagggaga ttggcaccta gtggctggga gcttgccagg
                                                                       240
aacccagtgg ccagggagcg tggcacttac ctttgtccct tgcttcattc ttgtgagatg
                                                                       300
ataaaactgg gcacagctct taaataaaat ataaatgaac a
                                                                       341
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      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature.
      <222> (1)...(844)
      <223> n = A, T, C or G
      <400> 132
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gaaccttcca gaagtgggca tctgtggtgg tgcctcttgg gaaggagcag aagtacacat
                                                                       120
gccatgtgga acatgagggg ctgcctgagc ccctcaccct gagatggggc aaggaggagc
                                                                       180
ctccttcatc caccaagact aacacagtaa tcattgctgt tccggttgtc cttggagctg
                                                                       240
tggtcatcct tggagctgtg atggcttttg tgatgaagag gaggagaaac acaggtggaa
                                                                       300
aaggagggga ctatgctctg gctccaggct cccagagctc tgatatqtct ctcccaqatt
                                                                       360
gtaaagtgtg aagacagctg cctggtgtgg acttggtgac agacaatgtc ttcacacatc
                                                                       420
tcctqtgaca tccagagacc tcagttctct ttagtcaagt gtctgatgtt ccctgtgagt
                                                                       480
ctgcgggctc aaagtgaaga actgtggagc ccagtccacc cctgcacacc aggaccctat
                                                                       540
ccctgcactg ccctgtgttc ccttccacag ccaaccttgc tgctccagcc aaacattggt
                                                                       600
```

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ggacatetge agectgtcag etecatgeta eeetgacett caacteetca ettecacaet
  gagaataata atttgaatgt gggtggctgg agagatggct cagcgctgac tgctcttcca
                                                                         660
  aaggteetga gtteaaatee cageaaceae atggtggete acaaceatet gtaatgggat
                                                                         720
  ctaataccct cttctgcagt gtctgaagac asctacagtg tacttacata taataataaa
                                                                         780
                                                                         840
                                                                         844
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        <211> 601
        <212> DNA
        <213> Homo sapien
        <400> 133
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 agcaagcagc gagtcttgaa gctctgtttg gtgctttgga tccatttcca tcggtcctta
                                                                         60
 cagccgctcg tcagactcca gcagccaaga tggtgaagca gatcgagagc aagactgctt
                                                                        120
 ttcaggaagc cttggacgct gcaggtgata aacttgtagt agttgacttc tcagccacgt
                                                                        180
 ggtgtgggcc ttgcaaaatg atcaagcctt tctttcattc cctctctgaa aagtattcca
                                                                        240
 acgtgatatt ccttgaagta gatgtggatg actgtcagga tgttgcttca gagtgtgaag
                                                                        300
 tcaaatgcat gccaacattc cagtttttta agaagggaca aaaggtgggt gaatttctg
                                                                        360
 gagccaataa ggaaaagctt gaagccacca ttaatgaatt agtctaatca tgttttctga
                                                                        420
 aaatataacc agccattggc tatttaaaac ttgtaatttt tttaatttac aaaaatataa
                                                                        480
 aatatgaaga cataaacccm gttgccatct gcgtgacaat aaaacattaa tgctaacact
                                                                        540
                                                                        600
                                                                        601
       <210> 134
       <211> 421
       <212> DNA
       <213> Homo sapien
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 agagaaaccc ttccctccct ccacctccct ccccaccct cctcatgaat taagaatcta
                                                                        60
 agagaagaag taaccataaa accaagtttt gtggaatcca tcatccagag tgcttacatg
                                                                       120
 gtgattaggt taatattgcc ttcttacaaa atttctattt taaaaaaaat tataaccttg
                                                                       180
attgcttatt acaaaaaaat tcagtacaaa agttcaatat attgaaaaat gcttttcccc
                                                                       240
tccctcacag caccgtttta tatatagcag agaataatga agagattgct agtctagatg
                                                                       300
gggcaatctt caaattacac caagacgcac agtggtttat ttaccctccc cttctcataa
                                                                       360
                                                                       420
                                                                       421
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      <211> 511
      <212> DNA
      <213> Homo sapien
      <400> 135
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gctgacagac aaagagagag agatggcgga aataagggat caaatgcagc aacagctgaa
                                                                       60
tgactatgaa cagcttettg atgtaaagtt agceetggae atggaaatca gtgettacag
                                                                       120
gaaactetta gaaggegaag aagagggtt gaagetgtet ceaagecett etteeegtgt
                                                                       180
gacagtatee egageateet caagtegtag tgtacegtae aactagagga aageggaaga
                                                                       240
gggttgatgt ggaagaatca gaggcgaagt agtagtgtta gcatctctca ttccgcctca
                                                                      300
accactggaa atgtttgcat cgaagaaatt gatgttgatg ggaaatttat cccgcttgaa
                                                                      360
gaacacttct gaacaggatc aaccaatggg aaggcttggg agatgatcag aaaaattgga
                                                                      420
gacacatcag tcagttataa atatacctca a
                                                                      480
                                                                      511
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<210> 136
     <211> 341
     <212> DNA
     <213> Homo sapien
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gecteggeet eccaaagtge tgggattaca ggegtgagee accaegeeeg geeeccaaag
                                                                    120
ctgtttcttt tgtctttagc gtaaagctct cctgccatgc agtatctaca taactgacgt
                                                                    180
gactgccagc aagctcagtc actccgtggt ctttttctct ttccagttct tctctctct
                                                                    240
ttcaagttct gcctcagtga aagctgcagg tccccagtta agtgatcagg tgagggttct
                                                                    300
ttgaacctgg ttctatcagt cgaattaatc cttcatgatg q
                                                                    341
     <210> 137
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     <212> DNA
     <213> Homo sapien
     <400> 137
gargiging accepting teaaaaaaaa ceteacaaag aateeesige teattacaga
                                                                     60
agaagatgca tttaaaatat gggttatttt caacttttta tctgaggaca agtatccatt
                                                                    120
aattattgtg tcagaagaga ttgaatacct gcttaagaag cttacagaag ctatgggagg
                                                                    180
aggttggcag caagaacaat ttgaacatta taaaatcaac tttgatgaca gtaaaaatgg
                                                                    240
cctttctgca tgggaactta ttgagcttat tggaaatgga cagtttagca aaggcatgga
                                                                    300
ccggcagact gtgtctatgg caattaatga agtctttaat gaacttatat tagatgtgtt
                                                                    360
aaagcagggt tacatgatga aaaagggcca cagacggaaa aactggactg aaagatggtt
                                                                    420
tgtactaaaa cccaacataa tttcttacta tgtgagtgag gatctgaagg ataagaaagg
                                                                    480
agacattete ttggatgaaa attgetgtgt agaagteett geetgacaaa agatggaaag
                                                                    540
aaatgccttt t
                                                                    551
     <210> 138
     <211> 531
     <212> DNA
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     <220>
     <221> misc_feature
     <222> (1)...(531)
     <223> n = A, T, C or G
      <400> 138
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                                                                     60
ttgatttctc tttctcccaa tcggccccaa agagaccaca taaaaggaga gtacatttta
                                                                    120
agccaataag ctgcaggatg tacacctaac agacctccta gaaaccttac cagaaaatgg
                                                                    180
ggactgggta gggaaggaaa cttaaaagat caacaaactg ccagcccacg gactgcagag
                                                                    240
300
atataaaatt taaaaagttt tgtacataag ctattcaaga tttctccagc actgactgat
                                                                    360
acaaagcaca attgagatgg cacttctaga gacagcagct tcaaacccag aaaagggtga
                                                                    420
tgagatgaag tttcacatgg ctaaatcagt ggcaaaaaca cagtcttctt tctttctttc
                                                                    480
tttcaaggan gcaggaaagc aattaagtgg tcaccttaac ataaggggga c
                                                                    531
      <210> 139
     <211> 521
      <212> DNA
      <213> Homo sapien
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<220>
       <221> misc_feature
        <222> (1)...(521)
       <223> n = A, T, C or G
       <400> 139
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 ctgcagcagc aggcagatga tgcagaggag cgagctgagc gcctccagcg agaagttgag
                                                                         60
 ggagaaaggc gggcccggga acaggctgag gctgaggtgg cctccttgaa ccgtaggatc
                                                                        120
 cagetggttg aagaagaget ggacegtget caggagegee tggecactge cetgeaaaag
                                                                        180
 ctggaagaag ctgaaaaagc tgctgatgag agtgagagag gtatgaaggt tattgaaaac
                                                                        240
 cgggccttaa aagatgaaga aaagatggaa ctccaggaaa tccaactcaa agaagctaag
                                                                        300
 cacattgcag aagaggcaga taggaagtat gaagaggtgg ctcgtaagtt ggtgatcatt
                                                                        360
 gaaggagact tggaaccgca cagaaggaac gagcttgagc ttggcaaaag tcccgttgcc
                                                                        420
                                                                        480
 cagagatggg atgaaccaga ttagactgat ggaccanaac c
                                                                        521
       <210> 140
       <211> 571
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(571)
       <223> n = A, T, C or G
       <400> 140
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ctggaagcgc cccgagagtg acagcgtgag gctgggaggg aggacttggc ttgagcttgt
                                                                       120
taaactctgc tctgagcctc cttgtcgcct gcatttagat ggctcccgca aagaagggtg
gcgagaagaa aaagggccgt tctgccatca acgaagtggt aacccgagaa tacaccatca
                                                                       180
acattcacaa gcgcatccat ggagtgggct tcaagaagcg tgcacctcgg gcactcaaag
                                                                       240
agatteggaa atttgccatg aaggagatgg gaactecaga tgtgcgcatt gacaccagge
                                                                       300
                                                                       360
tcaacaaagc tgtctgggcc aaaggaataa ggaatgtgcc ataccgaatc cggtgtgcgg
ctgtccagaa aacgtaatga ggatgaagat tcaccaaata agctatatac tttggttacc
                                                                       420
                                                                       480
tatgracetg ttaccacttt caaaaatcta cagacagtca atgtggatga gaactaatcg
                                                                       540
ctgatcgtca gatcaaataa agttataaaa t
                                                                       571
      <210> 141
      <211> 531
      <212> DNA
      <213> Homo sapien
      <400> 141
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aatggggagg cctcttggag acacagaggg tttcaccttg gatgacctct agagaaattg
                                                                       120
cccaagaagc ccaccttctg gtcccaacct gcagaccca cagcagtcag ttggtcaggc
                                                                       180
cetgetgtag aaggteactt ggeteeattg eetgetteea accaatggge aggagagaag
                                                                       240
gcctttattt ctcgcccacc cattcctcct gtaccagcac ctccgttttc agtcagtgtt
                                                                       300
gtccagcaac ggtaccgttt acacagtcac ctcagacaca ccatttcacc tcccttgcca
agctgttagc cttagagtga ttgcagtgaa cactgtttac acaccgtgaa tccattccca
                                                                       360
                                                                       420
tcagtccatt ccagttggca ccagcctgaa ccatttggta cctggtgtta actggagtcc
                                                                       480
tgtttacaag gtggagtcgg ggcttgctga cttctcttca tttgagggca c
                                                                       531
```

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<210> 142
      <211> 491
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(491)
      <223> n = A, T, C or G
      <400> 142
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ttgtcctgaa accctactgg agaagtcagc atgaggcacc tactgagaga agtgcccaga
                                                                       120
aactgctgac tgcatctgtt aagagttaac agtaaagagg tagaagtgtg tttctgaatc
                                                                       180
agagtggaag cgtctcaagg gtcccacagt ggaggtccct gagctacctc ccttccgtga
                                                                       240
gtgggaagag tgaagcccat gaagaactga gatgaagcaa ggatggggtt cctgggctcc
                                                                       300
aggcaagggc tgtgctctct gcagcaggga gccccacgag tcagaagaaa agaactaatc
                                                                       360
atttgttgca agaaaccttg cccggatact agcggaaaac tggaggcggn ggtgggggca
                                                                       420
caqqaaaqtq qaagtgattt gatggagagc agagaagcct atgcacagtg gccgagtcca
                                                                       480
cttgtaaagt g
                                                                       491
      <210> 143
      <211> 515
      <212> DNA
      <213> Homo sapien
      <400> 143
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tttccagttg ctattttcca aattgttctg taatgtcgtt aaaaattactt aaaaattaac
                                                                       120
aaaqccaaaa attatatta tgacaagaaa gccatcccta cattaatctt acttttccac
                                                                       180
tcaccggccc atctccttcc tctttttcct aactatgcca ttaaaactgt tctactgggc
                                                                       240
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gtactttgac cttagggtag aaggcaaagc tgccagtaaa tgtctcagca ttgctgctaa
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ttttggtcct gctagtttct ggattgtaca aataaatgtg ttgtagatga
                                                                      950
      <210> 163
      <211> 475
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(475)
      <223> n = A, T, C or G
      <400> 163
tegageggee geeegggeag gtgteggagt ceageaeggg aggegtqqte ttqtaqttqt
                                                                       60
tctccggctg cccattgctc tcccactcca cggcgatgtc gctgggatag aagcctttga
                                                                      120
ccaggcaggt caggctgacc tggttcttgg tcatctcctc ccgggatqqq qqcaqqqtqt
                                                                      180
acacctgtgg ttctcggggc tgccctttgg ctttggagat ggttttctcg atgggggctg
                                                                      240
ggagggcttt gttggagacc ttgcacttgt actccttgcc attcaaccag tcctggtqca
                                                                      300
```

```
ngacggtgag gacgctnacc acacggtacg ngctggtgta ctgctcctcc cgcggctttg
   tettggcatt atgcacetee acgcegteea egtaceaatt gaacttgace teagggtett
                                                                          360
   egtggeteac gtecaccacc acgeatgtaa ecteaaanet eggnegegan caege
                                                                          420
                                                                          475
         <210> 164
         <211> 476
         <212> DNA
         <213> Homo sapien
         <400> 164
  agcgtggtcg cggccgaggt ctgaggttac atgcgtggtg gtggacgtga gccacgaaga
  ccctgaggtc aagttcaact ggtacgtgga cggcgtggag gtgcataatg ccaagacaaa
                                                                          60
  geogegggag gageagtaca acageacgta ecgtgtggte agegteetea ecgteetgea
                                                                         120
  ccaggactgg ctgaatggca aggagtacaa gtgcaaggtc tccaacaaag ccctcccagc
                                                                         180
  ccccatcgag aaaaccatct ccaaagccaa agggcagccc cgagaaccac aggtgtacac
                                                                         240
  cetgececea tecegggagg agatgaceaa gaaceaggte ageetgacet geetggteaa
                                                                         300
  aggettetat eccagegaca tegecegtgg agtgggagag caatgggcag eeggagaaca
                                                                         360
  actacaagac cacgcctccc gtgctggact ccgacacctg ccgggcggcc gctcga
                                                                         420
                                                                         47.6
        <210> 165
        <211> 256
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
       <222> (1)...(256)
       <223> n = A, T, C or G
       <400> 165
 agcgtggttn cggccgaggt cccaaccaag gctgcancct ggatgccatc aaagtcttct
 gcaacatgga gactggtgag acctgcgtgt accccactca gcccagtgtg gcccagaaga
                                                                         60
 actggtacat cagcaagaac cccaaggaca agaggcatgt ctggttcggc gagagcatga
                                                                        120
ccgatggatt ccagttcgag tatggcggcc agggctccga ccctgccgat gtggacctgc
                                                                        180
                                                                        240
                                                                        256
       <210> 166
       <211> 332
       <212> DNA
      <213> Homo sapien
      <400> 166
agcgtggtcg cggccgaggt caagaacccc gcccgcacct gccgtgacct caagatgtgc
cactetgact ggaagagtgg agagtactgg attgacccca accaaggetg caacetggat
                                                                        60
gccatcaaag tettetgeaa catggagact ggtgagacet gegtgtacee cacteageee
                                                                       120
agtgtggccc agaagaactg gtacatcagc aagaacccca aggacaagag gcatgtctgg
                                                                       180
ttcggcgaga gcatgaccga tggattccag ttcgagtatg gcggccaggg ctccgacct
                                                                       240
gccgatgtgg acctgcccgg gcggccgctc ga
                                                                       300
                                                                       332
      <210> 167
      <211> 332
      <212> DNA
      <213> Homo sapien
      <220>
```

```
3.
      <221> misc feature
      <222> (1)...(332)
      <223> n = A, T, C or G
      <400> 167
togagoggtc gcccgggcag gtccacatcg gcagggtcgg agccctggcc gccatactcg
                                                                        60
aactggaatc categgneat getetegeeg aaccagaeat geetettgne ettggggtte
                                                                       120
ttgctgatgt accagnictt ctgggccaca ctgggctgag tggggtacac gcaggictca
                                                                       180
ccanteteca tgttgcanaa gaetttgatg gcatecaggt tgcageettg gttggggtca
                                                                       240
atccagtact ctccactctt ccagacagag tggcacatct tgaggtcacg gcaggtgcgg
                                                                       300
gcggggttct tgacctcggt cgcgaccacg ct
                                                                       332
      <210> 168
      <211> 276
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(276)
      <223> n = A, T, C or G
      <400> 168
togagoggco gooogggcag gtootootoa gagoggtago tqttottatt goooggcag
                                                                        60
cctccataga tnaagttatt gcangagttc ctctccacgt caaagtacca gcgtgggaag
                                                                       120
gatgcacggc aaggcccagt gactgcgttg gcggtgcagt attcttcata gttgaacata
                                                                       180
tegetggagt ggaetteaga ateetgeett etgggageae ttgggaeaga ggaateeget
                                                                       240
gcattcctgc tggtggacct cggccgcgac cacgct
                                                                       276
      <210> 169
      <211> 276
      <212> DNA
      <213> Homo sapien
      <400> 169
agcgtggtcg cggccgaggt ccaccagcag gaatgcagcg gattcctctg tcccaagtgc
                                                                        60
tcccagaagg caggattctg aagaccactc cagcgatatg ttcaactatg aagaatactg
                                                                       120
caccgccaac gcagtcactg ggccttgccg tgcatccttc ccacgctggt actttgacgt
                                                                       180
ggagaggaac tcctgcaata acttcatcta tggaggctgc cggggcaata agaacagcta
                                                                       240
ccgctctgag gaggacctgc ccgggcggcc gctcga
                                                                       276
      <210> 170
      <211> 332
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(332)
      <223> n = A, T, C or G
      <400> 170
togagoggco geologica gtecacateg geagggtegg ageologic geolatacteg
                                                                        60
aactggaatc catcggtcat gctctcgccg aaccagacat gcctcttgtc cttggggttc
                                                                       120
ttgctgatgt accagttctt ctgggccaca ctgggctgag tggggtacac gcaggtctca
```

180

```
ccagtctcca tgttgcagaa gactttgatg gcatccaggt tgcagccttg gttggggtca
   atccagtact ctccactctt ccagccagaa tggcacatct tgaggtcacg gcangtgcgg
                                                                          240
   gcggggttct tgacctcggc cgcgaccacg ct
                                                                          300
                                                                          332
         <210> 171
         <211> 333
         <212> DNA
         <213> Homo sapien
         <400> 171
  agcgtggtcg cggccgaggt caagaaaccc cgcccgcacc tgccgtgacc tcaagatgtg
  ccactetgge tggaagagtg gagagtactg gattgacccc aaccaagget gcaacctgga
                                                                          60
  tgccatcaaa gtcttctgca acatggagac tggtgagacc tgcgtgtacc ccactcagcc
                                                                         120
  cagtgtggcc cagaagaact ggtacatcag caagaacccc aaggacaaga ggcatgtctg
                                                                         180
  geteggegag ageatgaceg atggatteca gttegagtat ggeggeeagg geteegacee
                                                                         240
  tgccgatgtg gacctgcccg ggcggccgct cga
                                                                         300
                                                                         333
        <210> 172
        <211> 527
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(527)
        <223> n = A, T, C or G
       <400> 172
 agcgtggtcg cggccgaggt cctgtcagag tggcactggt agaagntcca ggaaccctga
 actgtaaggg ttcttcatca gtgccaacag gatgacatga aatgatgtac tcagaagtgt
                                                                         60
 cctgnaatgg ggcccatgan atggttgnct gagagagagc ttcttgtcct acattcggcg
                                                                        120
 ggtatggtct tggcctatgc cttatggggg tggccgttgn gggcggtgng gtccgcctaa
                                                                        180
 aaccatgttc ctcaaagatc atttgttgcc caacactggg ttgctgacca naagtgccag
                                                                        240
 gaagctgaat accatttcca gtgtcatacc cagggtgggt gacgaaaggg gtcttttgaa
                                                                        300
 ctgtggaagg aacatccaag atctctgntc catgaagatt ggggtgtgga agggttacca
                                                                        360
 gttggggaag ctcgctgtct ttttccttcc aatcangggc tcgctcttct gaatattctt
                                                                        420
 cagggcaatg acataaattg tatattcggt tcccggttcc aggccag
                                                                        480
                                                                        527
       <210> 173
       <211> 635
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(635)
      <223> n = A,T,C or G
      <400> 173
tegageggee geeegggeag gtecaceaea eccaatteet tgetggtate atggeageeg
ccacgtgcca ggattaccgg ctacatcatc aagtatgaga agcctgggtc tcctcccaga
                                                                        60
gaagtggtee cteggeeceg ecetggtgte acagaggeta ctattactgg cetggaaceg
                                                                       120
ggaaccgaat atacaattta tgtcattgcc ctgaagaata atcagaagag cgagcccctg
                                                                       180
attggaagga aaaagacaga cgagcttccc caactggtaa cccttccaca ccccaatctt
                                                                       240
catggaccag agatettgga tgtteettee acagtteaaa agacceettt egteacceae
                                                                       300
                                                                      360
```

```
cctgggtatg acactggaaa tggtattcag cttcctggca cttctggtca gcaacccagt
                                                                       420
gttgggcaac aaatgatctt tgangaacat ggntttaggc ggaccacacc ggccacaacg
                                                                       480
qqcaccccca taaggcatag gccaagaaca tacccgncga atgtaggaca agaagctctn
                                                                       540
teteanacaa neateteatg ggeeceatte cangacaett etgagtaeat cantteatgg
                                                                       600
catcctggtg gcactgataa aaacccttac agtta
                                                                       635
      <210> 174
      <211> 572
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(572)
      <223> n = A, T, C or G
      <400> 174
agcgtggtcg cgggcgaggt cctgtcagag tggcactggt agaagttcca ggaaccctga
                                                                        60
actgtaaggg ttcttcatca grgccaacag gatgacatga aatgatgtac tcagaagtgt
                                                                       120
cctggaatgg ggcccatgag atggttgtct gagagagagc ttcttgtcct acattcggcg
                                                                       180
ggtatggtct tggcctatgc cttatggggg tggccgttgt gggcggtgtg gtccgcctaa
                                                                       240
aaccatgttc ctcaaagatc atttgttgcc caacactggg ttgctgacca gaagtqccaq
                                                                       300
gaagctgaat accatttcca gtgtcatacc cagggtgggt gacgaaaggg qtcttttqaa
                                                                       360
ctgtggaagg aacatccaag atctctggtc catgaagatt ggggtgtgga agggttacca
                                                                       420
gttggggaag ctcgtctgtc tttttccttc caatcanggg ctcgctcttc tgattattct
                                                                       480
tcagggcaat gacataaatt gtatattcgg ntcccgggtn cagccaataa taataaccct
                                                                       540
ctgtgacacc anggcggggc cgaagganca ct
                                                                       572
      <210> 175
      <211> 372
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (372)
      <223> n = A, T, C or G
      <400> 175
agcgtggtcg cggccgaggt cctcaccaga ggtaccacct acaacatcat agtggaggca
                                                                        60
ctgaaagacc agcagaggca taaggttcgg gaagaggttg ttaccgtggg caactctgtc
                                                                       120
aacgaaggct tgaaccaacc tacggatgac tcgtgctttg acccctacac agtttcccat
                                                                       180
tatqccgttg gagatgagtg ggaacgaatg tctgaatcag gctttaaact gttgtgccag
                                                                       240
tgcttangct ttggaagtgg tcatttcaga tgtgattcat ctagatggtg ccatgacaat
                                                                       300
ggtgtgaact acaagattgg agagaagtgg gaccgtcagg gagaaaatgg acctgcccgg
                                                                       360
gcggccgctc ga
                                                                       372
      <210> 176
      <211> 372
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(372)
```

```
<223> n = A, T, C or G
        <400> 176
  togagoggoo gooogggoag gtocatttto toootgaogg toocaettot otocaatott
  gtagttcaca ccattgtcat ggcaccatct agatgaatca catctgaaat gaccacttcc
                                                                          60
  aaagcctaag cactggcaca acagtttaaa gcctgattca gacattcgtt cccactcatc
                                                                         120
  tccaacggca taatgggaaa ctgtgtaggg gtcaaagcac gagtcatccg taggttggtt
                                                                         180
 caageetteg ntgacagagt tgeceaeggt aacaacetet teeegaacet tatgeetetg
                                                                         240
 ctggtctttc agtgcctcca ctatgatgtt gtaggtggta cctctggtga ggacctcggc
                                                                         300
                                                                         360
                                                                         372
       <210> 177
       <211> 269
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(269)
       <223> n = A, T, C or G
       <400> 177
 agcgtggccg cggccgaggt ccattggctg gaacggcatc aacttggaag ccagtgatcg
 teteageett ggtteteeag etaatggtga tggnggtete agtageatet gteacacgag
                                                                         60
 cccttcttgg tgggctgaca ttctccagag tggtgacaac accctgagct ggtctgcttg
                                                                        120
 tcaaagtgtc cttaagagca tagacactca cttcatattt ggcgnccacc ataagtcctg
                                                                        180
 atacaaccac ggaatgacct gtcaggaac
                                                                        240
                                                                        269
       <210> 178
       <211> 529
       <212> DNA
      <213> Homo sapien
      <400> 178
tegageggee geeegggeag gteeteagae egggttetga gtacaeagte agtgtggttg
cettgeacga tgatatggag agceagecec tgattggaac ceagtecaca getatteetg
                                                                        60
caccaactga cctgaagttc actcaggtca cacccacaag cctgagcgcc cagtggacac
                                                                       120
cacccaatgt teageteact ggatategag tgegggtgae ceceaaggag aagaceggae
                                                                       180
caatgaaaga aatcaacctt gctcctgaca gctcatccgt ggttgtatca ggacttatgg
                                                                       240
cggccaccaa atatgaagtg agtgtctatg ctcttaagga cactttgaca agcagaccag
                                                                       300
ctcagggtgt tgtcaccact ctggagaatg tcagcccacc aagaagggct cgtgtgacag
                                                                       360
atgctactga gaccaccatc accattagct ggagaaccaa gactgagacg atcactggct
                                                                       420
tecaagttga tgeegtteea geeaatggae eteggeegeg accaegett
                                                                       480
                                                                       529
      <210> 179
      <211> 454
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
     <222> (1)...(454)
     <223> n = A, T, C or G
     <400> 179
```

```
agcgtggtcg cggccgaggt ctggccgaac tgccagtgta cagggaagat gtacatgtta
                                                                        60
tagntettet egaagteeeg ggeeageage teeaeggggt ggteteetge eteeaggege
                                                                       120
ttctcattct catggatctt cttcacccgc agcttctgct tctcagtcag aaggttgttg
                                                                       180
tcctcatccc tctcatacag ggtgaccagg acgttcttga gccagtcccg catgcgcagg
                                                                       240
gggaattcgg tcagctcaga gtccaggcaa ggggggatgt atttgcaagg cccgatgtag
                                                                       300
tccaagtgga gcttgtggcc cttcttggtg ccctccaagg tgcactttgt ggcaaagaag
                                                                       360
tggcaggaag agtcgaaggt cttgttgtca ttgctgcaca ccttctcaaa ctcgccaatg
                                                                       420
ggggctgggc agacctgccc gggcggccgc tcga
                                                                       454
      <210> 180
      <211> 454
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(454)
      <223> n = A, T, C or G
      <400> 180
tcgagcggcc gcccgggcag gtctgcccag cccccattgg cgagtttgag aaggngtgca
                                                                        60
gcaatgacaa caagacette gactetteet gccacttett tgccacaaag tgcaceetgg
                                                                       120
agggcaccaa gaagggccac aagctccacc tggactacat cgggccttgc aaatacatcc
                                                                       180
ccccttgcct ggactctgag ctgaccgaat tccccctgcg catgcgggac tggctcaaga
                                                                       240
acgtcctggt caccctgtat gagagggatg aggacaacaa ccttctgact gagaagcana
                                                                       300
agctgcgggt gaagaanatc catgagaatg anaagcgcct gnaggcanga gaccaccccg
                                                                       360
tggagctgct ggcccgggac ttcgagaaga actataacat gtacatcttc cctgtacact
                                                                       420
ggcagttcgg ccagacctcg gccgcgacca cgct
                                                                       454
      <210> 181
      <211> 102
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(102)
      <223> n = A, T, C or G
      <400> 181
agcgtggntg cggacgacgc ccacaaagcc attgtatgta gttttanttc agctgcaaan
                                                                        60
aataccncca gcatccacct tactaaccag catatgcaga ca
                                                                       102
      <210> 182
      <211> 337
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(337)
      <223> n = A, T, C or G
      <400> 182
tcgagcggtc gcccgggcag gtctgggcgg atagcaccgg gcatattttg gaatggatga
```

```
ggtctggcac cctgagcagc ccagcgagga cttggtctta gttgagcaat ttggctagga
  ggatagtatg cagcacggtt ctgagtctgt gggatagctg ccatgaagna acctgaagga
                                                                         120
  ggcgctggct ggtangggtt gattacaggg ctgggaacag ctcgtacact tgccattctc
                                                                         180
  tgcatatact ggntagtgag gcgagcctgg cgctcttctt tgcgctgagc taaagctaca
                                                                         240
  tacaatggct ttgnggacct cggccgcgac cacgctt
                                                                         300
                                                                         337
        <210> 183
        <211> 374
       <212> DNA
       <213> Homo sapien
       <400> 183
 togagogge geoogggeag gtocatttte teectgacgg toccaettet etecaatett
 gtagttcaca ccattgtcat gacaccatct agatgaatca catctgaaat gaccacttcc
                                                                         60
 aaagcctaag cactggcaca acagtttaaa gcctgattca gacattcgtt cccactcatc
                                                                        120
 tecaaeggea taatgggaaa etgtgtaggg gteaaageae gagteateeg taggttggtt
                                                                        180
 caagcetteg ttgacagaag ttgcccaegg taacaacete ttcccgaace ttatgcctet
                                                                        240
 gctggtcttt caagtgcctc cactatgatg ttgtaggtgg cacctctggt gaggacctcg
                                                                        300
                                                                        360
 gccgcgacca cgct
                                                                        374
       <210> 184
       <211> 375
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(375)
       <223> n = A, T, C or G
       <400> 184
agegtggttt geggeegagg teeteacean aggtgeeace tacaacatea tagtggagge
actgaaagac cagcagaggc ataaggttcg ggaagaggtt gttaccgtgg gcaactctgt
                                                                         60
caacgaagge ttgaaccaae etaeggatga etegtgettt gacceetaea eagntteeea
                                                                        120
ttatgccgtt ggagatgagt gggaacgaat gtctgaatca ggctttaaac tgttgtgcca
                                                                        180
gtgcttangc tttggaagtg gtcatttcag atgtgattca tctanatggt gtcatgacaa
                                                                        240
tggtgngaac tacaagattg gagagaagtg gnaccgtcag ggganaaaat ggacctgccc
                                                                        300
                                                                        360
gggcggcncg ctcga
                                                                        375
      <210> 185
      <211> 148
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(148)
      <223> n = A, T, C or G
      <400> 185
agcgtggteg eggeegaggt etggettnet geteangiga ttateetgaa eeateeagge
caaataagcg ccggctatgc ccctgnattg gattgccaca cggctcacat tgcatgcaag
                                                                        60
                                                                       120
tttgctgagc tgaaggaaaa gattgatc
                                                                       148
      <210> 186
```

```
<211> 397
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(397)
      <223> n = A, T, C or G
      <400> 186
tcgagcggcc gcccgggcag gtccaattga aacaaacagt tctgagaccg ttcttccacc
                                                                        60
actgattaag agtggggngg cgggtattag ggataatatt catttagcct tctgagcttt
                                                                       120
ctgggcagac ttggtgacct tgccagctcc agcagccttc tggtccactg ctttgatgac
                                                                       180
acccaccgca actgtctgtc tcatatcacg aacagcaaag cgacccaaag gtggatagtc
                                                                       240
tgagaagete teaacacaca tgggettgee aggaaccata teaacaatqq qeaqeateac
                                                                       300
cagacttcaa gaatttaagg gccatcttcc agctttttac cagaacggcg atcaatcttt
                                                                       360
tccttcagct cagcaaactt gcatgcaatg tgagccg
                                                                       397
      <210> 187
      <211> 584
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(584)
      <223> n = A, T, C or G
      <400> 187
tcgagcggcc gcccgggcag gtccagaggg ctgtgctgaa gtttgctgct gccactggag
                                                                        60
ccactccaat tgctggccgc ttcactcctg gaaccttcac taaccagatc caggcagcct
                                                                       120
tccgggagcc acggettett gtggntactg accccaggge tgaccaccag cetetcacgg
                                                                       180
aggcatctta tgttaaccta cctaccattg cgctgtgtaa cacagattct cctctqcgct
                                                                       240
atgtggacat tgccatccca tgcaacaaca agggagctca ctcagnqqqq tttqatqtqq
                                                                       300
tggatgctgg ctcgggaagt tctgcgcatg cgtggcacca tttcccgtga acacccatgg
                                                                       360
gangneatge etgatetgga ettetaeaga gateetgaag agattgaaaa agaagaacag
                                                                       420
gctgnttgct ganaaagcaa gtgaccaagg angaaatttc angggtgaaa nggactgctc
                                                                       480
ccgctcctga attcactgct actcaacctg angntgcaga ctggtcttga aggngnacan
                                                                       540
gggccctctg ggcctattta agcancttcg gtcgcgaaca cgnt
                                                                       584
      <210> 188
      <211> 579
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(579)
      <223> n = A, T, C or G
      <400> 188
agcgtgngtc gcggccgagg tgctgaatag gcacagaggg cacctgtaca ccttcagacc
                                                                        60
agtctgcaac ctcaggctga gtagcagtga actcaggagc gggagcagtc cattcaccct
                                                                       120
gaaattcctc cttggncact gccttctcag cagcagcctg ctcttcttt tcaatctctt
                                                                       180
caggatetet gtagaagtac agateaggea tgaceteeca tgggtgttea egggaaatgg
                                                                       240
```

```
tgccacgcat gcgcagaact tcccgagcca gcatccacca catcaaaccc actgagtgag
  ctcccttgtt gttgcatggg atgggcaatg tccacatagc gcagaggaga atctgtgtta
                                                                         300
  cacagogoaa tggtaggtag gttaacataa gatgootoog ogagaagotg gtggtoagoo
                                                                         360
  ctggggtcaa gtaaccacaa gaagccgtgg ctcccggaag gctgcctgga tctggttagt
                                                                         420
  gaaggntcca ggagtgaagc ggccaacaat tggagtggct tcagtggcaa gcagcaaact
                                                                         480
  teageacaag ceetetggae etgeeeggeg geegetega
                                                                         540
                                                                         579
        <210> 189
        <211> 374
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(374)
        <223> n = A, T, C or G
       <400> 189
 tegageggee geeegggeag gtecatttte teeetgaegg neeeacttet etecaatett
 gtagttcaca ccattgtcat ggcaccatct agatgaatca catctgaaat gaccacttcc
                                                                         60
 aaagcctaag cactggcaca acagtttaaa gcctgattca gacattcgtt cccactcatc
                                                                        120
 tecaaeggea taatgggaaa etgtgtaggg gteaaageae gagteateeg taggttggtt
                                                                        180
 caageetteg ttgacagagt tgeccaeggt aacaaceten teeecgaace ttatgeetet
                                                                        240
 getgggettt cagngeetee actatgatgn tgtagggggg cacetetggn gangaceteg
                                                                        300
 gccgcgacca cgct
                                                                        360
                                                                        374
       <210> 190
       <211> 373
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(373)
      <223> n = A,T,C or G
      <400> 190
agcgtggtcg cggccgaggt cctcaccaga ggtgccacct acaacatcat agtggaggca
ctgaaagacc agcagaggca taaggctcgg gaagaggttg ttaccgtggg caactctgtc
                                                                        60
aacgaagget tgaaccaace tacggatgac tegtgetttg acceetacac agttteccat
                                                                       120
tatgccgttg gagatgagtg ggaacgaatg tctgaatcag gctttaaact gttgtgccag
                                                                       180
tgcttangct ttggaagtgg gtcatttcag atgtgattca tctagatggt gccatgacaa
                                                                       240
tggngngaac tacaagattg gagagaagtg gnaccgncag ggagaaaatg gacctgcccg
                                                                       300
                                                                       360
                                                                       373
      <210> 191
      <211> 354
      <212> DNA
      <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(354)
     <223> n = A, T, C \text{ or } G
```

```
<400> 191
agcgtggtcg cggccgaggt ccacatcggc agggtcggag ccctggccgc catactcgaa
                                                                        60
ctggaatcca tcggtcatgc tctcgccgaa ccagacatgc ctcttgtcct tggggttctt
                                                                       120
gctgatgtac cagttettet gggecacact gggetgagtg gggtacacge aggteteace
                                                                       180
agtctccatg ttgcagaaga ctttgatggc atccaggntg caaccttggt tggggtcaat
                                                                       240
ccagtactct ccactcttcc agccagagtg gcacatcttg aggtcacggc aggtgcggnc
                                                                       300
gggggntttt gcggctgccc tctggncttc ggntgtnctc natctgctgg ctca
                                                                       354
      <210> 192
      <211> 587
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(587)
      <223> n = A, T, C or G
      <400> 192
tegageggee geeegggeag gtetegeggt egeactggtg atgetggtee tgttggteee
                                                                        60
cccggccctc ctggacctcc tggcccccct ggtcctccca gcgctggttt cgacttcagc
                                                                       120
ttcctgcccc agccacctca agagaaggct cacgatggtg gccgctacta ccgggctgat
                                                                       180
gatgccaatg tggttcgtga ccgtgacctc gaggtggaca ccaccctcaa gagcctgagc
                                                                       240
cagcagatcg agaacatccg gagcccagag ggcagncgca agaaccccgc ccgcacctgc
                                                                       300
cgtgacctca agatgtgcca ctctgactgg aagagtggag agtactggat tgaccccaac
                                                                       360
caagctgcaa cctggatgcc atcaaagtct tctgcaacat ggagactggt gagacctgcg
                                                                       420
tgtaccccac tcagcccagt gtggcccaaa agaactggta catcagcaag aaccccaagg
                                                                       480
acaagaagca tgtctggttc ggcgagaaca tgaccgatgg attccagttc gagtatggcg
                                                                       540
ggcagggctc cgaccctgcc gatggggacc ttggccgcga acacgct
                                                                       587
      <210> 193
      <211> 98
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(98)
      <223> n = A, T, C or G
      <400> 193
agcgtggnng cggccgaggt ataaatatcc agnccatatc ctccctccac acgctganag
                                                                        60
atgaagctgt ncaaagatct cagggtggan aaaaccat
                                                                        98
      <210> 194
      <211> 240
      <212> DNA
      <213> Homo sapien
      <400> 194
tcgagcggcc gcccgggcag gtccttcaga cttggactgt gtcacactgc caggcttcca
                                                                        60
gggctccaac ttgcagacgg cctgttgtgg gacagtctct gtaatcgcga aagcaaccat
                                                                       120
ggaagacctg ggggaaaaca ccatggtttt atccaccctg agatctttga acaacttcat
                                                                       180
ctctcagcgt gcggagggag gctctggact ggatatttct acctcggccq cqaccacqct
                                                                       240
```

```
<210> 195
          <211> 400
          <212> DNA
         <213> Homo sapien
         <220>
         <221> misc_feature
         <222> (1)...(400)
         <223> n = A, T, C or G
         <400> 195
   cgagcgggcg accgggcagg tncagactcc aatccanana accatcaagc cagatgtcag
  aagctacacc atcacaggtt tacaaccagg cactgactac aaganctacc tgcacacctt
  gaatgacaat geteggaget eccetgtggt categaegee tecaetgeea tigatgeace
                                                                          60
  atccaacctg cgtttcctgg ccaccacac caattccttg ctggtatcat ggcagccgcc
                                                                         120
                                                                         180
  acgtgccagg attaccggta catcatenag tatganaagc ctgggcctcc tcccagagaa
                                                                         240
  gnggteeete ggeeeegee tgntgteeea naggntaeta ttaetgngee ngeaacegge
                                                                         300
  aaccgatatc nattttgnca ttggccttca acaataatta
                                                                         360
                                                                         400
        <210> 196
        <211> 494
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(494)
        <223> n = A,T,C or G
       <400> 196
 agcgtggttc gcggccgang tcctgtcaga gtggcactgg tagaagttcc aggaaccctg
 aactgtaagg gttcttcatc agngccaaca ggatgacatg aaatgatgta ctcagaagtg
                                                                         60
 tectggaatg gggeccatga gatggttgte tgagagagag ettettgnee tgtetttte
                                                                        120
 cttccaatca ggggctcgct cttctgatta ttcttcaggg caatgacata aattgtatat
                                                                        180
 tegggteeeg gnteeaggee agtaatagta neetetgtga caccagggeg gngeegaggg
                                                                        240
 accacttete tgggaggaga eccaggette teatacttga tgatgtaace ggtaateetg
                                                                        300
geacgtggcg gctgccatga taccagcaag gaattggggt gtggtggcca ggaaacgcag
                                                                       360
gttggatggn gcatcaatgg cagtggaggc cgtcgatgac cacaggggga gctccgacat
                                                                       420
                                                                       480
                                                                       494
      <210> 197
      <211> 118
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(118)
      <223> n = A,T,C or G
      <400> 197
agegtggneg eggeegaggt geagegeggg etgtgeeace ttetgetete tgeecaacga
taaggagggt neetgeeec aggagaacat taactnteec cageteggee tetgeegg
                                                                       60
                                                                      118
      <210> 198
```

```
<211> 403
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(403)
      <223> n = A, T, C or G
      <400> 198
tcgagcggcc gcccgggcag gttttttttg ctgaaagtgg ntactttatt ggntgggaaa
                                                                        60
gggagaaget gtggtcagcc caagagggaa tacagagncc cgaaaaaggg gagggcaggt
                                                                       120
gggctggaac cagacgcagg gccaggcaga aactttctct cctcactgct cagcctggtg
                                                                       180
gtggctggag ctcanaaatt gggagtgaca caggacacct tcccacagcc attgcgqcgg
                                                                       240
cattteatet ggecaggaca etggetgtee acetggeact ggtecegaca gaageeegag
                                                                       300
ctggggaaag ttaatgttca cctgggggca ggaaccctcc ttatcattgn gcagagagca
                                                                       360
gaaggtggca cagcccgcgc tgcacctcgg ccgcgaccac gct
                                                                       403
      <210> 199
      <211> 167
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(167)
      <223> n = A,T,C or G
      <400> 199
tcgagcggcc gcccgggcag gtccaccata agtcctgata caaccacgga tgagctgtca
                                                                        60
ggagcaaggt tgatttcttt cattggtccg gncttctcct tgggggncac ccgcactcga
                                                                       120
tatccagtga gctgaacatt gggtggcgtc cactgggcgc tcaggct
                                                                       167
      <210> 200
      <211> 252
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(252)
      <223> n = A, T, C or G
      <400> 200
tcgagcggtt cgcccgggca ggtccaccac acccaattcc ttgctggtat catggcagcc
                                                                        60
qccacgtgcc aggattaccg gctacatcat caagtatgag aagcctgggt ctcctcccag
                                                                       120
agaagcggtc cctcggcccc gccctggtgt cacagaggct actattactg gcctggaacc
                                                                       180
gggaaccgaa tatacaattt atgtcattgn cctgaagaat aatcannaan agcgancccc
                                                                       240
tgattggaag ga
                                                                       252
      <210> 201
      <211> 91
      <212> DNA
      <213> Homo sapien
```

```
<400> 201
  agcgtggtcg cggccgaggt tgtacaagct ttttttttt tttttttt tttttttt
  tttttttt tttttttt ttttttt t
                                                                          60
                                                                          91
        <210> 202
        <211> 368
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(368)
        <223> n = A, T, C or G
       <400> 202
 tegageggne geeegggeag gtetgeeaac accaagattg geeeeggeg catecacaca
 gtccgtgtgc ggggaggtaa caagaaatac cgtgccctga ggttggacgt ggggaatttc
                                                                         60
 teetgggget cagagtgttg tactegtaaa acaaggatea tegatgttgt etacaatgea
                                                                        120
 tctaataacg agctggttcg taccaagacc ctggtgaaga attgcatcgt gctcatcgac
                                                                        180
 agcacaccgt accgacagtg gtacgagtcc cactatgcgc tgcccctggg ccgcaagaag
                                                                        240
 ggagccaagc tgactcctga ggaagaagag attttaaaca aaaaacgatc taanaaaaaa
                                                                        300
                                                                       360
                                                                       368
       <210> 203
       <211> 340
       <212> DNA
       <213> Homo sapien
       <400> 203
agegtggteg eggeegaggt gaaatggtat teagetteet ggeacttetg gteageaace
cagtgttggg caacaaatga tctttgagga acatggtttt aggcggacca caccgcccac
                                                                        60
aacggccacc cccataaggc ataggccaag accatacccg ccgaatgtag gacaagaagc
                                                                       120
teteteteag acaaccatet catgggeece attecaggae acttetgagt acateattte
                                                                       180
atgtcatcct gttggcactg atgaagaacc cttacagttc agggttcctg gaacttctac
                                                                       240
cagtgccact ctgacaggac ctgcccgggc ggccgctcga
                                                                       300
                                                                       340
      <210> 204
      <211> 341
      <212> DNA
      <213> Homo sapien
      <400> 204
tegageggee geeegggeag gteetgteag agtggeactg gtagaagtte caggaaccet
gaactgtaag ggttcttcat cagtgccaac aggatgacat gaaatgatgt actcagaagt
                                                                       60
gtcctggaat ggggcccatg agatggttgt ctgagagaga gcttcttgtc ctacattcgg
                                                                      120
cgggtatggt cttggcctat gccttatggg ggtggccgtt gtgggcggtg tggtccgcct
                                                                      180
aaaaccatgt tcctcaaaga tcatttgttg cccaacactg ggttgctgac cagaagtgcc
                                                                      240
aggaagctga ataccatttc acctcggccg cgaccacgct a
                                                                      300
                                                                      341
      <210> 205
      <211> 770
      <212> DNA
      <213> Homo sapien
     <220>
```

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```
<221> misc_feature
      <222> (1)...(770)
      <223> n = A, T, C or G
      <400> 205
tegageggee geeegggeag gteteeette ttgeggeeca ggggeagege atagtgggae
                                                                        60
togtaccact gtoggtacgg tgtgctgtog atgagcacga tgcaattott caccagggto
                                                                       120
ttggtacgaa ccagctcgtt attagatgca ttgtagacaa catcgatgat ccttgtttta
                                                                       180
cgagtacaac actotgagoo ccaggagaaa ttooccaogt ccaacotcag ggcacggtat
                                                                       240
ttcttgttac ctccccgcac acggactgtg tggatgcggc gggggccaag ctgactcctg
                                                                       300
aggaagaaga gattttaaac aaaaaacgat ctaaaaaaat tcagaagaaa tatgatgaaa
                                                                       360
ggaaaaagaa tgccaaaatc agcagtctcc tggaggagca gttccagcag ggcaagcttc
                                                                       420
ttqcgtgcat cgcttcaagg ccgggacagt gtgaccgagc agatggctat gtgctagagg
                                                                       480
gcaaagaagt ggagttctat cttaagaaaa tcagggccca gaatggtgng tcttcaacta
                                                                       540
atccaaaggg gagtttcaga ccagtgcaat cagcaaaaac attgatactg ntggccaaat
                                                                       600
ttattggtgc agggcttgca cantangann ggctgggtct tggggcttgg attggnacaa
                                                                       660
getttggcag cettttettt ggttttgcca aaaacetttt gntgaagang anacetnggg
                                                                       720
cggacccctt aaccgattcc acnccnggng gcgttctang gncccncttg
                                                                       770
      <210> 206
      <211> 810
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(810)
      <223> n = A, T, C or G
      <400> 206
agcqtggtcg cggccgaggt ctgctgcttc agcgaagggt ttctggcata accaatgata
                                                                        60
aggetgecaa agactgttee aataccagea ecagaaccag ecaeteetae tgttgeagea
                                                                       120
cctgcaccaa taaatttggc agcagtatca atgtctctgc tgattgcact qqtctqaaac
                                                                       180
tccctttgga ttagctgaga cacaccattc tgggccctga ttttcctaag atagaactcc
                                                                       240
aactetttge cetetageac atagecatet geteggteac actgteeegg cettgaageg
                                                                       300
atgcacgcaa gaagcttgcc ctgctggaac tgctcctcca ggagactgct gattttggca
                                                                       360
ttctttttcc tttcatcata tttcttctga atttttttag atcgtttttt gtttaaaatc
                                                                       420
tettetteet caggagteag ettggeecee geegeateea caeagteegt gtgegggag
                                                                       480
gtaacaagaa ataccgtgcc ctgaggttgg acgtggggaa tttctcctgg ggctcagagt
                                                                       540
ggtgtactcg taaaacaagg atcatcgatg gtgnctacaa tgcatctaat aacgagctgg
                                                                       600
gtcggaccca aagaacctgg ngaanaaatg gatcgnctca tcgacaggac accgtacccg
                                                                       660
acaggggnac gantcccact atgcgcttgc ccctgggccg caanaaagga aaactgcccg
                                                                       720
ggcggccntc gaaagcccaa ttntggaaaa aatccatcac actgggnggc cngtcgagca
                                                                       780
tgcatntana ggggcccatt ccccctnann
                                                                       810
      <210> 207
      <211> 257
      <212> DNA
      <213> Homo sapien
      <400> 207
tegageggee geeegggeag gteeceaace aaggetgeaa eetggatgee ateaaagtet
                                                                        60
tctgcaacat ggagactggt gagacctgcg tgtaccccac tcagcccagt gtggcccaga
                                                                       120
agaactggta catcagcaag aaccccaagg acaagaggca tgtctggttc ggcgagagca
                                                                       180
tgaccgatgg attccagttc gagtatggcg gccagggctc cgaccctgcc gatgtggacc
                                                                       240
```

```
tcggccgcga ccacgct
                                                                         257
        <210> 208
        <211> 257
        <212> DNA
        <213> Homo sapien
        <400> 208
  agcgtggtcg cggccgaggt ccacateggc agggtcggag ccctggccgc catactcgaa
  ctggaatcca tcggtcatgc tctcgccgaa ccagacatgc ctcttgtcct tggggttctt
                                                                          60
  getgatgtac cagttettet gggccacact gggctgagtg gggtacacgc aggteteacc
                                                                         120
  agtotocatg ttgcagaaga ctttgatggc atccaggttg cagcottggt tggggacotg
                                                                         180
 cccgggcggc cgctcga
                                                                        240
                                                                        257
        <210> 209
        <211> 747
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(747)
       <223> n = A, T, C or G
       <400> 209
 togageggee geoegggeag gtecaccaca eccaatteet tgetggtate atggeageeg
 ccacgtgcca ggattaccgg ctacatcatc aagtatgaga agcctgggtc tcctcccaga
                                                                         60
 gaagtggtcc ctcggccccg ccc:ggtgtc acagaggcta ctattactgg cctggaaccg
                                                                        120
 ggaaccgaat atacaattta tgtcattgcc ctgaagaata atcagaagag cgagcccctg
                                                                        180
 attggaagga aaaagacaga cgagetteee caactggtaa eeetteeaca eeecaatett
                                                                        240
 catggaccag agatettgga tgtteettee acagtteaaa agaceeettt egteaceeae
                                                                        300
 cctgggtatg acactggaaa tggtattcag cttcctggca cttctggtca gcaacccagt
                                                                        360
 gttgggcaac aaatgatett tgaggaacat ggntttaggc ggaccacace gcccacaacg
                                                                        420
 gccacccca taaggcatag gccaagacca tacccgccga atgtaggaca agaagctntn
                                                                        480
 tntcanacac cathinatgg gooccattoc aggacactto tgagtacato atttatgnca
                                                                        540
 totgtggcac ttgatgaaaa coottacagt toagggttot ggaactttta coaggootnt
                                                                        600
 tacaggactn ggccggacnc cttaagccna ttncaccctg gggcgttcta nggtcccact
                                                                        660
 cgnncactgg ngaaaatggc tactgtn
                                                                        720
                                                                        747
      <210> 210
      <211> 872
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(872)
      <223> n = A, T, C or G
      <400> 210
agegtggteg eggeegaggt ceaetagagg tetgtgtgee attgeecagg cagagtetet
gegttacaaa eteetaggag ggettgetgt geggagggee tgetatggtg tgetgeggtt
                                                                        60
catcatggag agtggggcca aaggctgcga ggttgtggtg tetgngaaac teenaggaca
                                                                       120
ngagggctaa attccatgaa gtttgtggat ggcctgatga tccacaatcg gagaccctgt
                                                                       180
taactactac cgtctnaccn cctgctgtnc ncccccnttt ctgctnaana catngggntn
                                                                       240
                                                                       300
```

```
ntnettgnee nteettgggt ngaanatnna atngeetnee enttentane netaetngnt
                                                                       360
ccananttgg cctttaaana atccnccttg ccttnnncac tgttcanntn tttnntcgta
                                                                       420
aaccctatna nttnnattan atnntnnnnn nctcacccc ctcntcattn anccnatang
                                                                       480
ctnnnaantc cttnanncct cccncccnnt ncnctcntac tnantncttc tnncccatta
                                                                       540
cnnagetett tentttaana taatgnngee nngetetnea thtetaenat htgnnnaatn
                                                                       600
cccccncccc cnancgnntt tttgacctnn naacctcctt tcctcttccc tncnnaaatt
                                                                       660
ncnnanttcc nenttccnnc ntttcggntn ntcccatnct ttccannnct tcantctanc
                                                                       720
ncnctncaac ttatttcct ntcatccctt nttctttaca nnccccctnn tctactcnnc
                                                                       780
nnttncatta natttgaaac tnccacnnct anttncctcn ctctacnntt ttatttncg
                                                                       840
ntcnctctac ntaatanttt aatnanttnt cn
                                                                       872
      <210> 211
      <211> 517
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(517)
      <223> n = A, T, C or G
      <400> 211
tegageggee geeegggeag gtetgeeaag gagaeeetgt tatgetgtgg ggaetggetg
                                                                        60
gggcatggca ggcggctctg gcttcccacc cttctgttct gagatggggg tggtgggcag
                                                                       120
tatctcatct ttgggttcca caatgctcac gtggtcaggc aggggcttct tagggccaat
                                                                       180
cttaccagtt gggtcccagg gcagcatgat cttcaccttg atgcccagca caccctgtct
                                                                       240
qaqcaacacg tggcgcacaa gcagtgtcaa cgtagtaagt taacagggtc tccgctgtgg
                                                                       300
atcatcagge catecacaaa etteatggat ttageeetet gteeteggag ttteecagae
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accacaacct cgcagccttt ggccccactc tccatgatga accgcagcac accatagcag
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gccctccgca caagcaagcc ctcctaagaa tttgtaacgc ananactctg ctggcaatgg
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      <223> n = A, T, C or G
      <400> 212
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gattcacaga ttccaggggg gccaggagaa ccaggggacc ctggttgtcc tggaatacca
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gggtcaccat ttctcccagg aataccagga gggcctggat ctcccttggg qccttgaggt
                                                                      240
ccttgaccat taggagggcg agtaggagca gttggaggct gtgggcaaac tgcacaacat
                                                                      300
tetecaaatg gaattietgg gttggggcag tetaattett gateegteac atattatgte
                                                                      360
atcgcagaga acggatcctg agtcacagac acatatttgg catggttctg gcttccagac
                                                                       420
atctctatcc gncataggac tgaccaagat gggaacatcc tccttcaaca agcttnctgt
                                                                       480
tgtgccaaaa ataatagtgg gatgaagcag accgagaagt anccagctcc cctttttgca
                                                                      540
caaagentea teatgtetaa atateagaea tgagaettet ttgggcaaaa aaggagaaaa
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agaaaaagca gttcaaagta nccnccatca agttggttcc ttgcccnttc agcacccggg
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ccccgttata aaacacctng ggccggaccc ccctt
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        <212> DNA
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        <220>
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        <223> n = A, T, C or G
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                                                                         60
 gatatttaga catgatgagc tttgtgcaaa aggggagctg gctacttctc gctctgcttc
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 atcccactat tattttggca caacaggaag ctgttgaagg aggatgttcc catcttggtc
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 agtectatge ggatagagat gtetggaage cagaaceatg ceaaatatgt gtetgtgaet
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 caggatccgt tetetgcgat gacataatat gtgacgatca agaattagac tgccccaacc
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 cagaaattcc atttggagaa tgttgtgcag tttgcccaca gcctccaact gctcctactc
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 gccctcctaa tggtcaagga cctcaaggcc ccaagggaga tccaggccct cctggtattc
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 cccctggaat cnggngaatc atgccctact ggtcctcaaa ctattctccc anatgattca
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 tatgatgtca agtctgggat agcnagtang ganggactcg caggctattc tggaccanac
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 ctgccggggg ggcgttcgaa agcccgaatc tgcananntn cnttcacact ggcggccgtc
                                                                        660
 gagetgettt aaaagggeea tteeneettt agngnggggg antacaatta etnggeggeg
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 ttttanancg cgngnctggg aaat
                                                                       780
                                                                       804
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       <212> DNA
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       <221> misc_feature
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      <223> n = A, T, C or G
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gctgatgtac cagttettet gggecacact gggetgagtg gggtacacge aggteteace
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agtotocatg ttgcagaaga ctttgatggc atccaggttg cagcottggt tggggtcaat
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ccagtactct ccactcttcc agtcagagtg gcacatcttg aggtcacggc aggtgcgggc
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ggggttettg eggetgeeet etgggeteeg gatgtteteg atetgetgge teaggetett
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gagggtggtg tecacetega ggteaeggte acgaaceaea ttggeateat cageceggta
                                                                       360
gtageggeca ceategtgag cettetettg angtggetgg ggcaggaact gaagtegaaa
                                                                       420
ccagegetgg gaggaccagg gggaccaana ggtccaggaa gggcccgggg gggaccaaca
                                                                       480
ggaccagcat caccaagtgc gacccgcgag aacctgcccg gccgnccgct cgaa
                                                                       540
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      <210> 215
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      <212> DNA
      <213> Homo sapien
     <220>
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<221> misc_feature
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cccggccctc ctggacctcc tggtccccct ggtcctccca gcgctggttt cgacttcagc
                                                                       120
ttcctgcccc agccacctca agagaaggct cacgatggtg gccgctacta ccgggctgat
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gatgccaatg tggttcgtga ccgtgacctc gaggtggaca ccaccctcaa gagcctgagc
                                                                       240
cagcagateg agaacateeg gageecagag ggeageegea agaaceeege eegeacetge
                                                                       300
cgtgacctca agatgtgcca ctctgactgg aagagtggag agtactggat tgaccccaac
                                                                       360
caaggetgea acctggatge catcaaagte ttetgeaaca tggagaetgg tgagaeetge
                                                                       420
gtgtacccca ctcagcccag tgtggcccag aagaactggt acatcagcaa gaaccccaag
                                                                       480
gacaagaggc atgtctggtt cggcgagagc atgaccgatg gattccagtt cgagtatggc
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ggccagggct cccaccctgc cgatgtggac ctccggccgc gaccaccctt
                                                                       590
      <210> 216
      <211> 801
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(801)
      <223> n = A, T, C or G
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agggtgctcg tggtttccct ggaactcctg gacttcctgg cttcaaaggc attaggggac
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acaatggtct ggatggattg aagggacagc ccggtgctcc tggtgtgaag ggtgaacctg
                                                                       240
gtgcccctgg tgaaaatgga actccaggtc aaacaggagc ccgtgggctt cctggtgaga
                                                                       300
gaggaccgtg ttggtgcccc tggcccanac ctcggccgcg accacgctaa gcccgaattt
                                                                       360
ccagcacact ggnggccgtt actantggat ccgagctcgg taccaagctt ggcgtaatca
                                                                       420
tggtcatagc tgtttcctgn gtgaaattgt tatccgctca caatttcaca cancatacga
                                                                       480
agccggaaag cataaagtgt aaagccttgg ggtgctaatg agtgagctaa ctcncattaa
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attgcgttgc gctcactgcc cgcttttcca nnngggaaac cntqgcntng ccnqcttgcn
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ttaantgaaa tccgccnacc cccggggaaa agncggtttg cngtattggg gcnctttttc
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cctttcctcg gnttacttga nttantgggc tttggncgnt tcgggttgng gcgancnggt
                                                                       720
tcaacntcac nccaaaggng gnaanacggt tttcccanaa tccgggggnt ancccaangn
                                                                       780
aaaacatnng ncnaanggge t
                                                                       801
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      <221> misc_feature
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      <223> n = A, T, C or G
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tcacaccagg agcaccgggc tgtcccttca atccatncag accattgtgn cccctaatgc
   ctttgaagcc aggaagtcca ggagttccag ggaaaccacc gagcaccctg tggtccaaca
                                                                          180
   actectetet caccaggteg teegggtttt ecagggtgae catetteace ageettgeea
                                                                          240
   ggaggaccag caggaccagc gttaccaacc tgcccgggcg gccgctcga
                                                                          300
                                                                          349
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         <211> 372
         <212> DNA
         <213> Homo sapien
         <400> 218
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  gtagttcaca ccattgtcat ggcaccatct agatgaatca catctgaaat gaccacttcc
                                                                          60
  aaageetaag caetggeaca acagtttaaa geetgattea gaeattegtt eccaeteate
                                                                         120
  tecaaeggca taatgggaaa etgtgtaggg gteaaageae gagteateeg taggttggtt
                                                                         180
  caageetteg ttgacagagt tgeecaeggt aacaacetet teeegaacet tatgeetetg
                                                                         240
  ctggtctttc agtgcctcca ctatgatgtt gtaggtggca cctctggtga ggacctcggc
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                                                                         360
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                                                                         60
 aacgaagget tgaaccaace tacggatgae tegtgetttg acceetacae agttteccat
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 tatgccgttg gagatgagtg ggaacgaatg tctgaatcag gctttaaact gtrgtgccag
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 tgcttaggct ttggaagtgg tcatttcaag atgtgattca tctagatggt gccatgacaa
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       <211> 828
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
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       <223> n = A, T, C or G
       <400> 220
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geggeagttg teacagegee ageceegetg geetecaaag catgtgeagg ageaaatgge
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accgagatat teettetgee actgttetee taegtggtat gtetteecat categtaaca
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cgttgcctca tgagggtcac acttgaattc tccttttccg ttcccaagac atgtgcagct
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catttggctg gctctatagt ttggggaaag tttgttgaaa ctgtgccact gacctttact
                                                                       240
tcctccttct ctactggagc tttcgtacct tccacttctg ctgttggtaa aatggtggat
                                                                       300
cttctatcaa tttcattgac agtacccact tctcccaaac atccagggaa atagtgattt
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cagagcgatt aggagaacca aattatgggg cagaaataag gggcttttcc acaggttttc
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ctttggagga agatttcagt ggtgacttta aaagaatact caacagtgtc ttcatcccca
                                                                       480
tagcaaaaga agaaacngta aatgatggaa ngcttctgga gatgccnnca tttaagggac
                                                                       540
neccagaact teaceateta caggacetae tteagtttae annaagneae atantetgae
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                                                                       660
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tcanaaagga cccaagtagc nccatggnca gcacttinag ccttteecet ggggaaaann tacnttett aaaneetngg cenngaeece ettaagneea aattntggaa aantteentn ennetggggg gengttenae atgenttina agggeeeaat tneecent  <210> 221	720 780 828
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 cagecaceag agtggatget gtetgeacec ategteetga ceceaaaage cetggaetgg
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 cotacaccot ggacagggac agtototatg toaatggttt caccoatogg agototgtac
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 ccaccaccag caccggggtg gtcagcgagg agccattcaa cctgcccggg cggccgctcg
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       <212> DNA
       <213> Homo sapien
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 cctggaatgg ggcccatgag atggttgtct gagagagagc ttcttgtcct acattcggcg
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gaagctgaat accatttcca gtgtcatacc cagggtgggt gacgaaaggg gtcttttgaa
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ctgtggaagg aacatccaag atctctggtc catgaagatt ggggtgtgga agggttacca
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gttggggaag ctcgtctgtc tttttccttc caatcagggg ctcgctcttc tgattattct
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tcagggcaat gacataaatt gtatattcgg tcccggttcc aggccagtaa tagtagcctc
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tgtgacacca gggcggggcc gagggaccct tctnttggaa gagaccagct tctcatactt
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gatgatgagn ccggtaatcc tggcacgtgg nggttgcatg atnccaccaa ggaaatnggn
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                                                                       660
gggggnggac ctgcccggcg gccgttcnaa agcccaattc cacacattg gnggccgtac
                                                                       720
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      <213> Homo sapien
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acagttgggt agccaatctg cagacagaca ctggcaacat tgcggacacc ctccaggaag
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cgagaatgca gagtttcctc tgtgatatca agcacttcag ggttgtagat gctgccattg
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                                                                        60
gcccagcaac accaaggtgg acaagagagt tgagcccaaa tcttgtgaca aaactcacac
                                                                       120
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<210> 228										
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agegrages eggeegaggt ceteacities etectional geacegatag etgegetetg	60									
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	100									
aagtgaggac ctcggccgcg accacgct	180 208									

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         <212> DNA
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                                                                          60
  ttgctgatgt accagttctt ctgggccaca ctgggctgag tggggtacac gcaggtctca
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  ccagteteca tgttgcagaa gaetttgatg gcatccaggt tgcagcettg gttggggtca
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  atcoagtact ctccactctt ccagtcagag tggcacatct tgaggtcacg gcaggtgcgg
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  gcggggttct tgacctcggc cgcgaccacg ct
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        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
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        <223> n = A, T, C or G
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 cetgeegtga cetcaagatg tgecactetg actggaagag tggagagtac tggattgace
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       <213> Homo sapien
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       <223> n = A, T, C or G
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gtcactggcc gtggagacag ccccgcaagc agcaagccaa tttccattaa ttaccgaaca
                                                                       180
gaaattgaca aaccateeea gatgeaagtg accgatgtte aggacaacag cattagtgte
                                                                       240
aagtggctgc cttcaagttc ccctgttact ggttacagag taaccaccac tcccaaaaat
                                                                       300
ggaccaggac caacaaaac taaaactgca ggtccagatc aaacagaaat gactattgaa
                                                                       360
ggettgcage ceacagtgga gtatgtggtt aagtgtetat getcagaate caageggaga
                                                                       420
gaagtcagcc tctggttcag actgnaagta accaacattg atcgcctaaa ggactggcat
                                                                       480
teactgatgn ggatgeegat tecateaaaa ttgnttggga aaaceeacag gggcaagttt
                                                                       540
ncangtenag gnggacetae tegageeetg aggatggaat cettgactnt teettnneet
                                                                       600
gatggggaaa aaaaaccttn aaaacttgaa ggacctgccc gggcggccgt ncaaaaccca
                                                                       660
                                                                       720
```

```
attecacece ettgggggeg tteratgggn eccaetegga ecaaaettgg ggraan
                                                                       776
      <210> 235
      <211> 805
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(805)
      <223> n = A, T, C or G
      <400> 235
tegageggee geeegggeag gteettgeag etetgeagtg tettetteac cateaggtge
                                                                        60
agggaatage teatggatte cateeteagg getegagtag gteaceetgt acetggaaae
                                                                       120
ttgcccctgt gggctttccc aagcaatttt gatggaatcg gcatccacat cagtgaatgc
                                                                       180
cagteettta gggegateaa tgttggttae tgeagtetga accagagget gaetetetee
                                                                       240
gettggatte tgageataga cactaaceae atacteeact gtgggetgea ageetteaat
                                                                       300
agtcatttct gtttgatctg gacctgcagt tttagttttt gttggtcctg gtccattttt
                                                                       360
gggagtggtg gttactctgt aaccagtaac aggggaactt gaaggcagcc acttgacact
                                                                       420
aatgctgttg tcctgaacat cggtcacttg catctgggat ggtttgtcaa tttctgttcg
                                                                       480
gtaattaatg gaaattggct tgctgcttgc ggggcttgtc tccacggcca gtgacagcat
                                                                       540
acacagtgat ggtataatca actccaggtt taagccgctg atggtagctg aaacttrgct
                                                                       600
ccaggcacaa gtgaactcct gacagggcta tttcctnctg ttctccgtaa gtgatcctgt
                                                                       660
aatatctcac tgggacagca ggangcattc caaaacttcg ggcgngaccc cctaagccga
                                                                       720
attntgcaat atncatcaca ctggcgggcg ctcgancatt cattaaaagg cccaatcncc
                                                                       780
cctataggga gtntantaca attng
                                                                       805
      <210> 236
      <211> 262
      <212> DNA
      <213> Homo sapien
      <400> 236
tcgagcggcc gcccgggcag gtcacttttg gtttttggtc atqttcgqtt qqtcaaaqat
                                                                        60
aaaaactaag tttgagagat gaatgcaaag gaaaaaaata ttttccaaag tccatgtgaa
                                                                       120
attgtctccc attttttgg cttttgaggg ggttcagttt gggttgcttg tctgtttccg
                                                                       180
ggttggggg aaagttggtt gggtgggagg gagccaggtt gggatggagg gagtttacag
                                                                       240
gaagcagaca gggccaacgt cg
                                                                       262
      <210> 237
      <211> 372
      <212> DNA
      <213> Homo sapien
      <400> 237
agogtggtcg cggccgaggt cctcaccaga ggtgccacct acaacatcat agtggaggca
                                                                        60
ctgaaagacc agcagaggca taaggttcgg gaagaggttg ttaccgtggg caactctgtc
                                                                       120
aacgaaggct tgaaccaacc tacggatgac tcgtgctttg acccctacac agtttcccat
                                                                       180
tatgccgttg gagatgagtg ggaacgaatg tctgaatcag gctttaaact gttgtgccag
                                                                       240
tgcttaggct ttggaagtgg tcatttcaga tgtgattcat ctagatggtg ccatgacaat
                                                                       300
ggtgtgaact acaagattgg agagaagtgg gaccgtcagg gagaaaatgg acctgcccgg
                                                                       360
geggeegete ga
                                                                       372
```

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<211> 372
          <212> DNA
          <213> Homo sapien
         <400> 238
   tegageggee geeegggeag gtecatttte teeetgaegg teeeacttet etecaatett
   gtagttcaca ccattgtcat ggcaccatct agatgaatca catctgaaat gaccacttcc
                                                                           60
   aaageetaag caetggeaca acagtttaaa geetgattea gaeattegtt eecaeteate
                                                                          120
   tecaaeggca taatgggaaa etgtgtaggg gteaaageae gagteateeg taggttggtt
                                                                          180
   caageetteg ttgacagagt tgeccaeggt aacaacetet teecgaacet tatgeetetg
                                                                          240
   ctggtctttc agtgcctcca ctatgatgtt gtaggtggca cctctggtga ggacctcggc
                                                                          300
                                                                          360
                                                                          372
         <210> 239
         <211> 720
         <212> DNA
         <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(720)
        <223> n = A, T, C \text{ or } G
        <400> 239
  tegageggee geeegggeag gtecaccata agteetgata caaccaegga tgagetgtea
 ggagcaaggt tgatttcttt cattggtccg gtcttctcct tgggggtcac ccgcactcga
                                                                          60
 tatecagtga getgaacatt gggtggtgte caetgggege teaggettgt gggtgtgace
                                                                         120
 tgagtgaact tcaggtcagt tggtgcagga atagtggtta ctgcagtctg aaccagaggc
                                                                         180
 tgactetete egettggatt etgageatag acaetaacea cataeteeae tgtgggetge
                                                                         240
 aagcettcaa tagtcattte tgtttgatet ggacetgeag ttttagtttt tgttggteet
                                                                         300
 ggtccatttt tgggagtggt ggttactctg taaccagtaa caggggaact tgaaggcagc
                                                                         360
 cacttgacac taatgctgtt gtcctgaaca tcggtcactt gcatctggga tggtttgnca
                                                                         420
 atttctgttc ggtaattaat ggaaattggc ttgctgcttg cggggctgtc tccacggcca
                                                                        480
 gtgacagcat acacagngat ggnatnatca actccaagtt taaggccctg atggtaactt
                                                                        540
 taaacttgct cccagccagn gaactteegg acagggtatt tettetggtt tteegaaagn
                                                                        600
 gancetggaa tnnteteett ggancagaag ganenteeaa aacttgggee ggaaceeett
                                                                        660
                                                                        720
       <210> 240
       <211> 691
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(691)
      <223> n = A, T, C or G
      <400> 240
agcgtggtcg cggccgaggt cctgtcagag tggcactggt agaagttcca ggaaccctga
actgtaaggg ttcttcatca gtgccaacag gatgacatga aatgatgtac tcagaagtgt
                                                                        60
cetggaatgg ggcccatgag atggttgtet gagagagage ttettgteet acatteggeg
                                                                       120
ggtatggtet tggcctatgc cttatggggg tggccgttgt gggcggtgtg gtccgcctaa
                                                                       180
aaccatgtte ctcaaagate atttgttgee caacactggg ttgetgacea gaagtgeeag
                                                                       240
gaagetgaat accattteea gtgteatace eagggtgggt gaegaaaggg gtettttgaa
                                                                       300
ctgtggaagg aacatccaag atctctggtc catgaagatt ggggtgtgga agggttacca
                                                                       360
                                                                       420
```

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```
gttggggaag ctcgtctgtc tttttccttc caatcagggg ctcgctcttc tgattattct
                                                                       480
tcagggcaat gacataaatt gtatattcgg ttcccggttc caggccagta atagtagcct
                                                                       540
cttgtgacac caggcggggc ccanggacca cttctctggg angagaccca gcttctcata
                                                                       600
cttgatgatg taacccggta atcctgcacg tggcggctgn catgatacca ncaaggaatt
                                                                       660
gggtgnggng gacctgcccg gcggccctcn a
                                                                       691
      <210> 241
      <211> 808
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(808)
      <223> n = A, T, C or G
      <400> 241
agegtggteg eggeegaggt etgggatget eetgetgtea eagtgagata ttacaggate
                                                                        60
acttacggag aaacaggagg aaatagccct gtccaggagt tcactgtgcc tgggagcaag
                                                                       120
tctacageta ccatcagegg ccttaaacct ggagttgatt ataccatcac tgtgtatgct
                                                                       180
gtcactggcc gtggagacag ccccgcaagc agcaagccaa tttccattaa ttaccgaaca
                                                                       240
gaaattgaca aaccatccca gatgcaagtg accgatgttc aggacaacag cattagtgtc
                                                                       300
aagtggetge etteaagtte eeetgttaet ggttacagag taaccaccae teecaaaaat
                                                                       360
ggaccaggac caacaaaaac taaaactgca ggtccagatc aaacagaaat gactattgaa
                                                                       420
ggcttgcagc ccacagtgga gtatgtggtt agtgtctatg ctcagaatcc aagcggagag
                                                                       480
agtcagcctc tggttcagac tgcagtaacc actattcctg caccaactga cctgaagttc
                                                                       540
actcaggtca cacccacaag cctgagccgc cagtggacac cacccaatgt tcactcactg
                                                                       600
gatatcgagt gcgggtgacc cccaaggaga agacccggac ccatgaaaga aatcaacctt
                                                                       660
getectgaca geteatecgn gggtgtatea ggaettatgg gggaetgeee eggenggeeg
                                                                       720
ntcgaaancg aattntgaaa tttccttcnc actgggnggc gnttcgagct tncttntana
                                                                       780
nggcccaatt cncctntagn gggtcgtn
                                                                       808
      <210> 242
      <211> 26
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(26)
      <223> n = A, T, C or G
      <400> 242
agcgtggtcg cggccgaggt cnagga
                                                                        26
      <210> 243
      <211> 697
      <212> DNA
      <213> Homo sapien
      <220>
     <221> misc feature
      <222> (1)...(697)
      <223> n = A, T, C or G
```

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```
<400> 243
   tegageggee geeegggeag gteeaceaea eccaatteet tgetggtate atggeageeg
  ccacgtgcca ggattaccgg ctacatcatc aagtatgaga agcctgggtc tcctcccaga
                                                                          60
  gaagtggtee cteggeeceg ecetggtgte acagaggeta ctattactgg eetggaaceg
                                                                         120
  ggaaccgaat atacaattta tgtcattgcc ctgaagaata atcagaagag cgagccctg
                                                                         180
  attggaagga aaaagacaga cgagetteee caactggtaa eeetteeaca eeecaatett
                                                                         240
  catggaccag agatettgga tgtteettee acagtteaaa agaeeeettt egteaceeae
                                                                         300
  cctgggtatg acactggaaa tggtattcag cttcctggca cttctggtca gcaacccagt
                                                                         360
  gttgggcaac aaatgatett tgaggaacat ggttttagge ggaccacace geccacaacg
                                                                         420
  ggcaccccca taaggnatag gccaagacca taccccgccg aatgtaggac aagaagctct
                                                                         480
  nteteaacaa ceateteatg ggeeceatte caggacaett etgagtaeat cattteatgt
                                                                         540
  catectggtg ggcacttgat gaanaaccet tacagttcag ggttcctgga acttctacca
                                                                         600
  gngccacttc tgacagganc ttgggcgnga ccaccct
                                                                         660
                                                                         697
        <210> 244
        <211> 373
        <212> DNA
        <213> Homo sapien
        <400> 244
 agegtggteg eggeegaggt ceattitete eetgaeggte eeaettetet eeaatettgt
 agttcacacc attgtcatgg caccatctag atgaatcaca tctgaaatga ccacttccaa
                                                                         60
 agectaagea etggeacaac agtttaaage etgatteaga cattegttee eacteatete
                                                                        120
 caacggcata atgggaaact gtgtaggggt caaagcacga gtcatccgta ggttggttca
                                                                        180
 agcettegtt gacagagttg cccaeggtaa caacetette eegaacetta tgeetetget
                                                                        240
 ggtctttcag tgcctccact atgatgttgt aggtggcacc tctggtgagg acctgcccgg
                                                                        300
 geggeeeget ega
                                                                        360
                                                                        373
       <210> 245
       <211> 307
       <212> DNA
       <213> Homo sapien
       <400> 245
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 ctgetteetg taaacteect ecateceaac etggeteect eccaeceaac caacttteee
                                                                        60
cecaaccegg aaacagacaa gcaacccaaa etgaaccece teaaaagcca aaaaaatggg
                                                                       120
agacaatttc acatggactt tggaaaatat ttttttcctt tgcattcatc tctcaaactt
                                                                       180
agtttttatc tttgaccaac cgaacatgac caaaaaccaa aagtgacctg cccgggcggc
                                                                       240
                                                                       300
                                                                       307
      <210> 246
      <211> 372
      <212> DNA
      <213> Homo sapien
      <400> 246
tegageggee geeegggeag gteeteacea gaggtgeeac etacaacate atagtggagg
cactgaaaga ccagcagagg cataaggttc gggaagaggt tgttaccgtg ggcaactctg
                                                                        60
tcaacgaagg cttgaaccaa cctacggatg actcgtgctt tgacccctac acagtttccc
                                                                       120
attatgccgt tggagatgag tgggaacgaa tgtctgaatc aggctttaaa ctgttgtgcc
                                                                       180
agtgcttagg ctttggaagt ggtcatttca gatgtgattc atctagatgg tgccatgaca
                                                                       240
atggtgtgaa ctacaagatt ggagagaagt gggaccgtca gggagaaaat ggacctcggc
                                                                       300
cgcgaccacg ct
                                                                       360
                                                                       372
```

```
<210> 247
      <211> 348
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(348)
      <223> n = A, T, C or G
      <400> 247
tcgagcggcc gcccgggcag gtaccggggt ggtcagcgag gagccattca cactgaactt
                                                                        60
caccatcaac aacctgcggt atgaggagaa catgcagcac cctggctcca ggaagttcaa
                                                                       120
caccacggag agggtccttc agggcctgct caggtccctg ttcaagagca ccagtgttgg
                                                                       180
ccctctgtac tctggctgca gactgacttt gctcagacct gagaaacatg gggcagccac
                                                                       240
tggagtggac gccatctgca ccctccgcct tgatcccact ggtnctggac tggacanana
                                                                       300
geggetatac ttgggagetg ancenaacet ttggeggnga encenett
                                                                       348
      <210> 248
      <211> 304
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(304)
      <223> n = A, T, C \text{ or } G
      <400> 248
gaggactggc tcagctccca gtatagccgc tctctgtcca gtccaggacc agtgggatca
                                                                        60
aggeggaggg tgeagatgge gteeacteea gtggetgeec catgtttete aagtetgage
                                                                       120
aaagncagtc tgcagccaga gtacagaggg ccaacactgg tgctcttgaa cagggacctg
                                                                       180
agcaggccct gaaggaccct ctccgtggtg ttgaacttcc tqgagccagg gtgctgcatg
                                                                       240
ttctcctcat accgcaggtt gttgatggtg aagttcagtg tgaatggctc ctcgctqacc
                                                                       300
accc
                                                                        304
      <210> 249
      <211> 400
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(400)
      <223> n = A, T, C or G
      <400> 249
agcgtggtcg cggccgaggt ccaccacac caattecttg ctggtateat ggcagecgec
                                                                         60
acgtgccagg attaccggct acatcatcaa gtatgagaag cctgggtctc ctcccagaga
                                                                        120
agtggtccct cggccccgcc ctggtgtcac agaggctact attactggcc tggaaccggg
                                                                        180
aaccgaatat acaatttatg tcattgccct gaagaataat cagaagagcg agcccctgat
                                                                        240
tggaaggaaa aagacagacg agcttcccca actggtaacc cttccacacc ccaatcttca
                                                                        300
tggaccanan ancttggatn gtcctttcac nggttnaaaa aacccttttc qccccccac
                                                                        360
cttggggatt aaccttggga aanggggatt tnaccnttcc
                                                                        400
```

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```
<210> 250
        <211> 400
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(400)
        <223> n = A, T, C or G
        <400> 250
  tegageggee geeegggeag gteetgteag agtggeaetg gtagaagtte caggaaceet
  gaactgtaag ggttcttcat cagtgccaac aggatgacat gaaatgatgt actcagaagt
                                                                          60
 gtcctggaat ggggcccatg agatggttgt ctgagagaga gcttcttgtc ctacattcgg
                                                                         120
 cgggtatggt cttggcctat gccttatggg ggtggccgtt gtgggcggtg tggtccgcct
                                                                         180
 aaaaccatgt tootcaaaga toatttgttg occaacactg ggttgotgac cagaagtgoo
                                                                         240
 aggaagctga ataccatttc cagtgtcata cccagggngg gtgaccaaag ggggtcnttt
                                                                         300
 ngacetggng aaaggaacca tecaaaanet etgneecatg
                                                                        360
                                                                        400
       <210> 251
       <211> 514
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(514)
       <223> n = A, T, C or G
       <400> 251
 agcgtggncg cggccgaggt ctgaggatgt aaactcttcc caggggaagg ctgaagtgct
 gaccatggtg ctactgggtc cttctgagtc agatatgtga ctgatgngaa ctgaagtagg
                                                                         60
 tactgtagat ggtgaagtet gggtgteeet aaatgetgea teteeagage etteeateat
                                                                        120
taccgtttct tcttttgcta tgggatgaga cactgttgag tattctctaa agtcaccact
                                                                        180
gaaatcttcc tccaaaggaa aacctgtgga aaagcccctt atttctgccc cataatttgg
                                                                        240
ttetectaat enetetgaaa teaetattte eetggaangt ttgggaaaaa nngggenace
                                                                        300
tgncantgga aantggatan aaagatccca ccattttacc caacnagcag aaagtgggaa
                                                                        360
nggtaccgaa aagctccaag taanaaaaag gagggaagta aaggtcaagt gggcaccagt
                                                                        420
ttcaaacaaa actttcccca aactatanaa ccca
                                                                        480
                                                                        514
      <210> 252
      <211> 501
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(501)
      <223> n = A, T, C or G
      <400> 252
aageggeege eegggeaggn neagnagtge ettegggaet gggnteacee eeaggtetge
ggcagttgtc acagcgccag ccccgctggc ctccaaagca tgtgcaggag caaatggcac
                                                                        60
cgagatattc cttctgccac tgttctccta cgtggtatgt cttcccatca tcgtaacacg
                                                                       120
ttgcctcatg agggtcacac ttgaattctc cttttccgtt cccaagacat gtgcagctca
                                                                       180
                                                                       240
```

```
tttggctggc tctatagttt ggggaaagtt tgttgaaact gtgccactga cctttacttc
                                                                        300
ctccttctct actggagctt tccgtacctt ccacttctgc tgntggnaaa aagggnggaa
                                                                        360
cntettatea attteattgg acagtanece netttetnee caaaacatne aagggaaaat
                                                                        420
attgattnen agageggatt aaggaacaac eenaattatg ggggeeagaa ataaaggggg
                                                                        480
cttttccaca ggtnttttcc t
                                                                        501
      <210> 253
      <211> 226
      <212> DNA
      <213> Homo sapien
      <400> 253
tcgagcggcc gcccgggcag gtctgcaggc tattgtaagt gttctgagca catatgagat
                                                                        60
aacctgggcc aagctatgat gttcgatacg ttaggtgtat taaatgcact tttgactgcc
                                                                       120
atctcagtgg atgacagcct tctcactgac agcagagatc ttcctcactg tgccagtggg
                                                                       180
caggagaaag agcatgctgc gactggacct cggccgcgac cacqct
                                                                        226
      <210> 254
      <211> 226
      <212> DNA
      <213> Homo sapien
      <400> 254
agcgtggtcg cggccgaggt ccagtcgcag catgctcttt ctcctgccca ctggcacagt
                                                                        60
gaggaagatc tctgctgtca gtgagaaggc tgtcatccac tqagatqqca qtcaaaaqtq
                                                                       120
catttaatac acctaacgta tcgaacatca tagcttggcc caggttatct catatgtgct
                                                                       180
cagaacactt acaatagect geagacetge eegggeggee getega
                                                                       226
      <210> 255
      <211> 427
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(427)
      <223> n = A, T, C \text{ or } G
      <400> 255
cgagcggccg cccgggcagg tccagactcc aatccagaga accaccaagc cagatgtcag
                                                                        60
aagctacacc atcacaggtt tacaaccagg cactgactac aagatctacc tgtacacctt
                                                                        120
gaatgacaat geteggaget cecetgtggt categaegee tecaetgeea ttgatgeace
                                                                        180
atccaacctg cgtttcctgg ccaccacacc caattccttg ctggtatcat ggcagccgcc
                                                                        240
acqtqccagg attaccggct acatcatcaa gtatgagaag cctgggtctc ctcccagaga
                                                                        300
agtggtccct Cggccccgcc ctggtgncac agaagctact attactgqcc tggaaccqqq
                                                                       360
aaccgaatat acaatttatg tcattgccct gaagaataat canaagagcq agcccctgat
                                                                        420
tggaagg
                                                                        427
      <210> 256
      <211> 535
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
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<222> (1)...(535)
        <223> n = A, T, C or G
        <400> 256
 agcgtggtcg cggccgaggt ectgtcagag tggcactggt agaagttcca ggaaccctga
 actgtaaggg ttcttcatca gtgccaacag gatgacatga aatgatgtac tcagaagtgt
                                                                         60
 cctggaatgg ggcccatgag atggttgtct gagagagagc ttcttgtcct gtcttttcc
                                                                        120
 ttccaatcag gggctcgctc ttctgattat tcttcagggc aatgacataa attgtatatt
                                                                        180
 cggttcccgg ttccaggcca gtaatagtag cctctgtgac accagggcgg ggccgaggga
                                                                        240
 ccacttetet gggaggagac ccaggettet catacttgat gatgtanecg gtaateetgg
                                                                        300
 caccgtggcg gctgccatga taccagcaag gaattgggtg tggtggccaa gaaacgcagg
                                                                        360
 ttggatggtg catcaatggc agtggaggcg tcgatnacca caggggagct ccgancattg
                                                                        420
 tcattcaagg tggacaggta gaatcttgta atcaggtgcc tggtttgtaa acctg
                                                                        480
                                                                        535
       <210> 257
       <211> 544
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(544)
       <223> n = A, T, C or G
       <400> 257
tegageggee geeegggeag gtttegtgae egtgaeeteg aggtggaeae caeeeteaag
agectgagee ageagatega gaacateegg ageceagagg geageegeaa gaaceeegee
                                                                         60
cgcacctgcc gtgacctcaa gatgtgccac tctgactgga agagtggaga gtactggatt
                                                                       120
gaccccaacc aaggetgeaa cetggatgee atcaaagtet tetgeaacat ggagactggt
                                                                       180
gagacetgeg tgtaceceae teageceagt gtggeeeaga agaactggta cateageaag
                                                                       240
aaccccaagg acaagaagca tgtctggttc ggcgaaagca tgaccgatgg attccagttc
                                                                       300
gagtatggcg gccagggctc cgaccetgcc gatgtggacc tcggccgcga ccacgctaag
                                                                       360
cccgaattcc agcacactgg cggccgttac tagtgggatc cgagcttcgg taccaagctt
                                                                       420
ggcgtaatca tgggncatag ctgtttcctg ngtgaaaatg gtattccgct tcacaatttc
                                                                       480
                                                                       540
ccac
                                                                       544
      <210> 258
      <211> 418
      <212> DNA
      <213> Homo sapien
      <400> 258
agcgtggtcg cggccgaggt ccacatcggc agggtcggag ccctggccgc catactcgaa
ctggaatcca tcggtcatgc tctcgccgaa ccagacatgc ctcttgtcct tggggttctt
                                                                        60
gctgatgtac cagttettet gggccacact gggctgagtg gggtacacge aggtetcace
                                                                       120
agtetecatg ttgcagaaga etttgatgge atccaggttg cagcettggt tggggtcaat
                                                                       180
ccagtactct ccactettee agteagagtg gcacatettg aggteaegge aggtgeggge
                                                                       240
ggggttettg eggetgeect etgggeteeg gatgtteteg atetgetgge teaagetett
                                                                       300
gaagggtggt gtccacctcg aggtcacggt cacgaaacct gcccgggcgg ccgctcga
                                                                       360
                                                                       418
      <210> 259
      <211> 377
      <212> DNA
     <213> Homo sapien
```

```
<220>
     <221> misc_feature
     <222> (1)...(377)
     <223> n = A, T, C or G
     <400> 259
agegtggteg eggeegaggt caagaacece geeegeacet geegtgaeet caagatgtge
                                                                     60
cactetgact ggaagagtgg agagtactgg attgacccca accaaggetg caacetggat
                                                                    120
gccatcaaag tettetgcaa catggagaet ggtgagaeet gegtgtaeee caetcageee
                                                                    180
agtgtggccc agaagaactg gtacatcagc aagaacccca aggacaagag gcatgtctgg
                                                                    240
ttcggcgaga gcatgaccga tggattccag ttcgagtatg gcggccaggg ctccgaccct
                                                                    300
geogatgtgg acctgecegn geoggneege tegaaaagee enaattteea gneacacttg
                                                                    360
gccggccgtt actactg
                                                                    377
     <210> 260
     <211> 332
     <212> DNA
     <213> Homo sapien
     <400> 260
tcgagcggcc gcccgggcag gtccacatcg gcagggtcgg agccctggcc gccatactcg
                                                                     60.
aactggaatc catcggtcat gctctcgccg aaccagacat gcctcttgtc cttggggttc
                                                                    120
ttgctgatgt accagttctt ctgggccaca ctgggctgag tggggtacac gcaggtctca
                                                                    180
ccaqtctcca tgttgcagaa gactttgatg gcatccaggt tgcagccttg gttggggtca
                                                                    240
atccagtact ctccactctt ccagtcagag tggcacatct tgaggtcacg qcaggtgcgg
                                                                    300
gcggggttct tgacctcggc cgcgaccacg ct
                                                                    332
     <210> 261
     <211> 94
     <212> DNA
     <213> Homo sapien
     <400> 261
60
ttttttttt tttttttt ttttttttttttttt
                                                                     94
     <210> 262
     <211> 650
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(650)
     <223> n = A, T, C or G
     <400> 262
agcgtggtcg cggccgaggt ctggcattcc ttcgacttct ctccaqccga qcttcccaqa
                                                                     60
acatcacata tcactgcaaa aatagcattg catacatgga tcaggccagt ggaaatgtaa
                                                                    120
agaaggccct gaagctgatg gggtcaaatg aaggtgaatt caaggctgaa ggaaatagca
                                                                    180
aattcaccta cacagttctg gaggatggtt gcacgaaaca cactggggaa tggagcaaaa
                                                                    240
cagtctttga atatcgaaca cgcaaggctg tgagactacc tattgtagat attgcaccct
                                                                    300
atgacattgg tggtcctgat caagaatttg gtgtggacgt tggccctgtt tgcttttat
                                                                    360
aaaccaaact ctatctgaaa tcccaacaaa aaaaatttaa ctccatatgt qntcctcttg
                                                                    420
ttctaatctt ggcaaccagt gcaagtgacc gacaaaattc cagttattta tttccaaaat
                                                                    480
```

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```
gtttggaaac agtataattt gacaaagaaa aaaggatact tetettttt tggetggtee
 accaaataca attcaaaagg ctttttggtt ttatttttt anccaattcc aatttcaaaa
                                                                         540
 tgtctcaatg gngcttataa taaaataaac tttcaccctt nttttntgat
                                                                         600
                                                                         650
        <210> 263
        <211> 573
        <212> DNA
        <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(573)
       <223> n = A, T, C or G
       <400> 263
 agegtggteg eggeegaggt etgggatget eetgetgtea eagtgagata ttacaggate
 acttacggag aaacaggagg aaatagccct gtccaggagt tcactgtgcc tgggagcaag
                                                                         60
 tetacageta ccateagegg cettaaacet ggagttgatt ataceateae tgtgtatget
                                                                        120
 gtcactggcc gtggagacag ccccgcaagc agcaagccaa tttccattaa ttaccgaaca
                                                                        180
 gaaattgaca aaccateeca gatgcaagtg accgatgtte aggacaacag cattagtgte
                                                                        240
 aagtggetge etteaagtte eeetgttact ggttacagaa gtaaccacca eteccaaaaa
                                                                        300
 tggaccagga ccaacaaaaa ctaaaactgc aggtccagat caaacagaaa atggactatt
                                                                        360
gaaggettge ageceacagt ggaagtatgt ggntaggngt etatgeteag aateceaage
                                                                        420
cggagaaagt cagcettetg gtttagactg cagtaaccaa cattgatege cctaaaggac
                                                                        480
tggncattca cttggatggt ggatgtccaa ttc
                                                                        540
                                                                        573
      <210> 264
      <211> 550
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(550)
      <223> n = A, T, C or G
      <400> 264
tegageggee geeegggeag gteettgeag etetgeagng tettetteac cateaggtge
agggaatage teatggatte catecteagg getegagtag gteaccetgt acctggaaac
                                                                        60
ttgcccctgt gggctttccc aagcaatttt gatggaatcg acatccacat cagngaatgc
                                                                       120
cagteetta gggegateaa tgttggttac tgcagtetga accagagget gactetetec
                                                                       180
gettggatte tgageataga cactaaceae atacteeaet gtgggetgea ageetteaat
                                                                       240
agtcatttct gtttgatctg gacctgcagt tttaagtttt tggtggtcct gncccatttt
                                                                       300
tgggaagtgg ggggttactc tgtaaccagt aacaggggaa cttgaaggca gccacttgac
                                                                       360
actaatgctg ttgtcctgaa catcggtcac ttgcatctgg ggatggtttt gacaatttct
                                                                       420
ggttcggcaa attaatggaa attggcttgc tgcttggcgg ggctgnctcc acgggccagt
                                                                       480
                                                                       540
gacagcatac
                                                                      550
     <210> 265
     <211> 596
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
```

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```
<222> (1)...(596)
      <223> n = A, T, C or G
      <400> 265
tcgagcggcc gcccgggcag gtccttgcag ctctgcagtg tcttcttcac catcaggtgc
                                                                        60
agggaatage teatggatte cateeteagg getegagtag gteaceetgt acetggaaae
                                                                       120
ttgcccctgt gggctttccc aagcaatttt gatggaatcg acatccacat cagtgaatgc
                                                                       180
cagteettta gggegateaa tgttggttae tgeagtetga accagagget gaetetetee
                                                                       240
gettggatte tgageataga cactaaccae atactecaet gtgggetgea ageetteaat
                                                                       300
agtcatttct gtttgatctg gacctgcagt tttaagtttt tgttggncct gnnccatttt
                                                                       360
tggggaaggg gtggttactc ttgtaaccag taacagggga acttgaagca gccacttgac
                                                                       420
actaatgctg gtggcctgaa catcggtcac ttgcatctgg gatggtttgg tcaatttctg
                                                                       480
ttcggtaatt aatgggaaat tggcttactg gcttgcgggg gctgtctcca cggncagtga
                                                                       540
caagcataca caggngatgg gtataatcaa ctccaggttt aaggccnctg atggta
                                                                       596
      <210> 266
      <211> 506
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(506)
      <223> n = A, T, C or G
      <400> 266
agcgtggtcg cggccgaggt ctgggatgct cctgctgtca cagtgagata ttacaggatc
                                                                        60
acttacggag aaacaggagg aaatagccct gtccaggagt tcactgtgcc tgggagcaag
                                                                       120
tctacagcta ccatcagcgg ccttaaacct ggagttgatt ataccatcac tgtgtatgct
                                                                       180
gtcactggcc gtggagacag ccccgcaagc agtaagccaa tttccattaa ttaccgaaca
                                                                       240
qaaattgaca aaccatccca gatgcaagtg accgatgttc aggacaacag cattagtgtc
                                                                       300
aagtggctgc cttcaagttc ccctgttact ggttacagag taaccaccac tcccaaaaat
                                                                       360
gggaccagga ccaacaaaaa actaaaactg canggtccag atcaaacaga aatgactatt
                                                                       420
gaaggettge ageccacagt ggagtatgtg ggttagtgte tatgeteaga atnecaageg
                                                                       480
gagagagtca gcctctggtt cagact
                                                                       506
      <210> 267
      <211> 548
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(548)
      <223> n = A, T, C or G
      <400> 267
tcgagcggcc gcccgggcag gtcagcgctc tcaggacgtc accaccatgg cctgggctct
                                                                        60
gctcctcctc accctcctca ctcagggcac agggtcctgg gcccagtctg ccctgactca
                                                                       120
gcctccctcc gcgtccgggt ctcctggaca gtcagtcacc atctcctgca ctggaaccag
                                                                       180
cagtgacgtt ggtgcttatg aatttgtctc ctggtaccaa caacacccag gcaaggcccc
                                                                       240
caaactcatg atttctgagg tcactaagcg gccctcaggg gtccctgatc gcttctctgg
                                                                       300
ctccaagtct ggcaacacgg cctccctgac cgtctctggg ctccangctg aggatgangc
                                                                       360
tgattattac tggaagctca tatgcaggca acaacaattg ggtgttcggc ggaagggacc
                                                                       420
aagetgaceg tnetaaggte aageceaagg ettgeeece teggteacte tgtteecace
                                                                       480
```

```
ctcctctgaa gaagctttca agccaacaan gncacactgg gtgtgtctca taagtggact
                                                                         540
                                                                         548
        <210> 268
       <211> 584
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(584)
       <223> n = A, T, C or G
       <400> 268
 agcgtggtcg cggccgaggt ctgtagcttc tgtgggactt ccactgctca ggcgtcaggc
 tcaggtagct gctggccgcg tacttgttgt tgctttgntt ggagggtgtg gtggtctcca
                                                                         60
 ctcccgcctt gacggggctg ctatctgcct tccaggccac tgtcacggct cccgggtaga
                                                                        120
 agtcacttat gagacacacc agtgtggcct tgttggcttg aagctcctca gaggagggtg
                                                                        180
 ggaacagagt gaccgagggg gcagccttgg gctgacctag gacggtcagc ttggtcctc
                                                                        240
 cgccgaacac ccaattgttg ttgcctgcat atgagctgca gtaataatca gcctcatcct
                                                                        300
 cagectggag eccagagaen gteaagggag geeegtgttt geeaagaett ggaageeaga
                                                                        360
 naagcgatca gggacccctg agggccgctt tacngacctc aaaaaatcat gaatttgggg
                                                                        420
 ggcctttgcc tgggngttgg ttggtnacca gnaaaacaaa atttcataaa gcaccaacgt
                                                                        480
cactgctggt ttccagtgca ngaanatggt gaactgaant gtcc
                                                                        540
                                                                        584
       <210> 269
      <211> 368
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(368)
      <223> n = A, T, C or G
      <400> 269
agcgtggtcg cggccgaggt ccagcatcag gagccccgcc ttgccggctc tggtcatcgc
ctttcttttt gtggcctgaa acgatgtcat caattcgcag tagcagaact gccgtctcca
                                                                        60
ctgctgtctt ataagtctgc agcttcacag ccaatggctc ccatatgccc agttccttca
                                                                       120
tgtccaccaa agtacccgtc tcaccattta caccccaggt ctcacagttc tcctgggtgt
                                                                       180
gcttggcccg aagggaggta agtanacgga tggtgctggt cccacagttc tggatcaggg
                                                                       240
tacgaggaat gacctctagg gcctgggcna caagccctgt atggacctgc ccgggcgggc
                                                                       300
                                                                       360
ccgctcga
                                                                       368
      <210> 270
      <211> 368
      <212> DNA
      <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(368)
     <223> n = A, T, C or G
     <400> 270
```

```
tegageggee geeegggeag greeataeag ggergtrage caggeeerag aggneatree
                                                                        60
tigiaccity atccagaact gigggaccag caccatecgi ctacttacci ecciteggge
                                                                       120
caagcacacc caggagaact gtgagacctg gggtgtaaat ggngagacgg gtactttggt
                                                                       180
ggacatgaag gaactgggca tatgggagcc attggctgng aagctgcana cttataagac
                                                                       240
aqcagtqgag acggcagttc tgctactgcg aattgatgac atcgtttcag gccacaaaaa
                                                                       300
gaaaggegat gaccanagee ggeaaggegg ggetteetga tgetggaeet eggeegeega
                                                                       360
ccacqctt
                                                                       368
      <210> 271
      <211> 424
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(424)
      <223> n = A, T, C or G
      <400> 271
agcgtggtcg cggccgaggt ccactagagg tctgtgtgcc attgcccagg cagagtctct
                                                                        60
gcgttacaaa ctcctaggag gccttgctgt gcggagggcc tgctatggtg tgctgcggtt
                                                                       120
catcatggag agtggggcca aaggctgcga ggttgtggtg tctgggaaac tccgaggaca
                                                                       180
gagggctaaa tccatgaagt ttgtggatgg cctgatgatc cacagcggag accctgttaa
                                                                       240
ctactacgtt gacactgctg tgcgccacgt gttgctcana cagggtgtgc tgggcatcaa
                                                                       300
ggtgaagatc atgctgccct gggacccanc tggcaaaaat ggcccttaaa aaccccttgc
                                                                       360
cntgaccacg tgaaccattt gtgngaaccc caagatgaan atacttgccc accaccccc
                                                                       420
attc
                                                                       424
      <210> 272
      <211> 541
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(541)
      <223> n = A, T, C or G
      <400> 272
tcgagcggcc gcccgggcag gtctgccaag gagaccctgt tatgctgtgg ggactggctg
                                                                        60
gggcatggca ggcggctctg gcttcccacc cttctgttct gagatggggg tggtgggcag
                                                                       120
tatctcatct ttgggttcca caatgctcac gtggtcaggc aggggcttct tagggccaat
                                                                       180
cttaccagtt gggtcccagg gcagcatgat cttcaccttg atgcccagca caccctgtct
                                                                       240
gagcaacacg tggcgcacag cagtgtcaac gtagtagtta acagggtctc cgctgtggat
                                                                       300
catcaggcca tccacaaact tcatggattt agccctctgt cctcqqaqtt tcccaaaaca
                                                                       360
ccacaacctc gccagccttt gggccccact tcttcatgaa tgaaaccgca gcacaccatt
                                                                       420
ancaaggeee tteegeacag gnaageeett eetaaggagt tttgtaaaeg caaaaaaete
                                                                       480
ttgcctgggg caaatgggca cacagacctn tantnggacc ttggnccgcg aaccaccgct
                                                                       540
                                                                       541
      <210> 273
      <211> 579
      <212> DNA
      <213> Homo sapien
```

```
<220>
        <221> misc_feature
        <222> (1)...(579)
        <223> n = A, T, C or G
        <400> 273
  agcgtggtcg cggccgaggt ctggccctcc tggcaaggct ggtgaagatg gtcaccctgg
  aaaacccgga cgacctggtg agagaggagt tgttggacca cagggtgctc gtggtttccc
                                                                          60
  tggaactcct ggacttcctg gcttcaaagg cattagggga cacaatggtc tggatggatt
                                                                         120
  gaagggacag cccggtgctc ctggtgtgaa gggtgaacct ggngcccctg gtgaaaatgg
                                                                         180
  aactccaggt caaacaggag cccgngggct tcctggngag agaggacgtg ttggtgcccc
                                                                         240
  tggcccanac ctgcccgggc ggccgctcna aaagccgaaa tccagnacac tggcggccgn
                                                                         300
  tactantgga atccgaactt cggtaccaaa gcttggccgt aatcatggcc atagcttgtt
                                                                         360
  ccctggggng gaaattggta ttccgctncc aattccacac aacataccga acccggaaag
                                                                         420
 cattaaagtg taaaagccct gggggggcct aaatgangtg agcntaactc ncatttaatt
                                                                         480
 ggcgttgcgc ttcactgccc cgcttttcca gtccgggna
                                                                         540
                                                                         579
        <210> 274
        <211> 330
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(330)
       <223> n = A, T, C or G
       <400> 274
 tegageggee geeegggeag gtetgggeea ggggeaceaa caegteetet eteaceagga
 ageccacggg etectgtttg acctggagtt ccattttcac caggggcacc aggttcacce
                                                                         60
tteacaccag gageaccggg etgtecette aatecateca gaccattgtg necectaatg
                                                                        120
cctttgaagc caggaagtcc aggagttcca gggaaaccac gagcaccctg tggtccaaca
                                                                        180
actectetet caccaggteg teegggtttt ceagggtgac catetteace ageettgeea
                                                                        240
ggagggccag acctcggccg cgaccacgct
                                                                        300
                                                                        330
      <210> 275
      <211> 97
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(97)
      <223> n = A, T, C or G
      <400> 275
ancgtggtcg cggccgaggt cctcaccaga ggtgncacct acaacatcat agtggaggca
ctgaaagacc ancagaggca taaggttcgg gaagagg
                                                                        60
                                                                        97
      <210> 276
      <211> 610
      <212> DNA
      <213> Homo sapien
      <220>
```

```
<221> misc_feature
      <222> (1)...(610)
      <223> n = A, T, C or G
     <400> 276
togagoggco gocogggoag gtocatttto tocotgacgg toccacttot otocaatott
                                                                       60
gtagttcaca ccattgtcat ggcaccatct agatgaatca catctgaaat gaccacttcc
                                                                       120
aaagcctaag cactggcaca acagtttaaa gcctgattca gacattcgtt cccactcatc
                                                                       180
tccaacggca taatgggaaa ctgtgtaggg gtcaaagcac gagtcatccg taggttggtt
                                                                       240
caageetteg ttgacagagt tgtccaeggt aacaacetet teeegaacet tatgeetetg
                                                                       300
ctggtctttc agtgcctcca ctatgatgtt gtaggtggca cctctggtga ggacctcngn
                                                                       360
congaacaac gottaagooc gnattotgoa gaataatooc atcacacttg goggoogott
                                                                       420
cgancatgca tcntaaaagg ggccccaatt tcccccttat aagngaancc gtatttncca
                                                                       480
atttcactgg necegocgnt tttacaaacg neggtgaact ggggaaaaac cetqqeqqtt
                                                                       540
acccaacttt aatcgccntt ggcagcacaa tcccccttt tcgnccancn tgggcgtaaa
                                                                       600
taaccgaaaa
                                                                       610
      <210> 277
      <211> 38
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(38)
      <223> n = A, T, C or G
      <400> 277
                                                                        38
ancgnggtcg cggccgangt ntttttttt
      <210> 278
      <211> 443
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(443)
      <223> n = A, T, C or G
      <400> 278
agcgtggtcg cggccgaggt ctgaggttac atgcgtggtg gtggacgtga gccacgaaga
                                                                        60
ccctgaggtc aagttcaact ggtacgtgga cggcgtggag gtgcataatg ccaagacaaa
                                                                       120
gccgcgggag gagcagtaca acagcacgta ccgggnggtc agcgtcctca ccgtcctgca
                                                                       180
ccagaattgg ttgaatggca aggagtacaa gngcaaggtt tccaacaaag ccntcccagc
                                                                       240
ccccntcgaa aaaaccattt ccaaagccaa agggcagccc cgagaaccac aggtgtacac
                                                                       300
cctgcccca tcccgggagg aaaagancaa naaccnggtt cagccttaac ttgcttggtc
                                                                       360
naangetttt tateecaaeg naetteecee ntggaantgg gaaaaaceaa tgggeeaane
                                                                       420
cgaaaaacaa ttacaanaac ccc
                                                                       443
      <210> 279
      <211> 348
      <212> DNA
      <213> Homo sapien
```

```
<220>
        <221> misc_feature
        <222> (1)...(348)
        <223> n = A, T, C or G
        <400> 279
 tcgagcggcc gcccgggcag gtgtcggagt ccagcacggg aggcgtggtc ttgtagttgt
 tetecggetg cecattgete teccaeteca eggegatgte getgggatag aageetttga
                                                                          60
 ccaggcaggt caggctgacc tggttcttgg tcatctcctc ccgggatggg ggcagggtga
                                                                         120
 acacctgggg ttctcggggc ttgccctttg gttttgaana tggttttctc gatgggggct
                                                                         180
 ggaagggctt tgttgnaaac cttgcacttg actccttgcc attcacccag ncctggngca
                                                                         240
 ggacggngag gacnetnace acacggaace gggetggtgg actgetce
                                                                         300
                                                                         348
       <210> 280
       <211> 149
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(149)
       <223> n = A, T, C or G
       <400> 280
agcgtggtcg cggacgangt cctgtcagag tggnactggt agaagttcca ngaaccctga
actgtaaggg ttcttcatca gtgccaacag gatgacatga aatgatgtac tcagaagngn
                                                                         60
 cctggaatgg ggcccatgan atggttgcc
                                                                        120
                                                                        149
       <210> 281
       <211> 404
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(404)
      <223> n = A, T, C or G
      <400> 281
tcgagcggcc gcccgggcag gtccaccaca cccaattcct tgctggtatc atggcagccg
ccacgtgcca ggattaccgg ctacatcatc aagtatgaga agcctgggtc tcctcccaga
                                                                        60
gaagtggtcc ctcggccccg ccctggtgtc acagaggcta ctattactgg cctggaaccg
                                                                       120
ggaaccgaat atacaattta tgtcattgcc ctgaagaata atcagaagag cgagccctg
                                                                       180
attggaagga aaaagacaga cgagcttccc caactggtaa cccttccaca ccccaatctt
                                                                       240
catggaccag agatettgga tgtteettee acagtteaaa agaeeeettt eggeaeeeee
                                                                       300
cctgggtatg aacctgggaa aanggnantt aancttteet ggca
                                                                       360
                                                                       404
      <210> 282
      <211> 507
      <212> DNA
      <213> Homo sapien
      <220>
     <221> misc_feature
     <222> (1)...(507)
```

```
<223> n = A, T, C \text{ or } G
      <400> 282
agcgtggtcg cggccgaggt ctgggatgct cctgctgtca cagtgagata ttacaggatc
                                                                         60
acttacggag aaacaggagg aaatagccct gtccaggagt tcactgtgcc tgggagcaag
                                                                        120
tctacagcta ccatcagcgg ccttaaacct ggagttgatt ataccatcac tgtgtatgct
                                                                        180
gtcactggcc gtggagacag ccccgcaagc agcaagccaa tttccattaa ttaccgaaca
                                                                        240
gaaattgaca aaccatccca gatgcaagtg accgatgttc aggacaacag cattagtgtc
                                                                        300
aagtggetge etteaaggtn eeetggtaet gggttacaga ntaaccaeca eteccaaaaa
                                                                        360
tqqaccaqga accacaaaaa cttaaactgc agggtccaga tcaaaacaga aatgactatt
                                                                        420
gaangettgc agcccacagt gggagtatgn gggtagtgnc tatgcttcag aatccaagcg
                                                                        480
gaaaaangtc aagccttntg ggttcaa
                                                                        507
      <210> 283
      <211> 325
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(325)
      <223> n = A, T, C or G
      <400> 283
togagoggeo geoogggeag gtoottgeag ctotgeagtg tottotteac cateaggtge
                                                                         60
aqqqaatagc tcatggattc catcctcagg gctcgagtag gtcaccctgt acctggaaac
                                                                        120
ttgcccctgt gggctttccc aagcaatttt gatggaatcg acatccacat cagtgaatgc
                                                                        180
cagteettta gggegateaa tgttggttae tgeagnetga accagagget gaetetetee
                                                                        240
gcttggattc tgagcataga cactaaccac atactccact gtgggctgca ancettcaat
                                                                        300
aanncatttc tgtttgatct ggacc
                                                                        325
      <210> 284
      <211> 331
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(331)
      <223> n = A, T, C or G
      <400> 284
tcgagcggcc gcccgggcag gtctggtggg gtcctggcac acgcacatgg gggngttgnt
                                                                         60
ctnatccagc tgcccagccc ccattggcga gtttgagaag gtgtgcagca atgacaacaa
                                                                        120
naccttcgac tcttcctgcc acttctttgc cacaaagtgc accctggagg gcaccaagaa
                                                                        180
gggccacaag ctccacctgg actacatcgg gccttgcaaa tacatccccc cttgcctgga
                                                                        240
ctctgagctg accgaattcc cccttgcgca tgcgggactg gctcaagaac cgtcctggca
                                                                        300
cccttgtatg anagggatga agacacnacc c
                                                                        331
      <210> 285
      <211> 509
      <212> DNA
      <213> Homo sapien
      <220>
```

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```
<221> misc feature
        <222> (1)...(509)
       \langle 223 \rangle n = A, T, C or G
       <400> 285
 agcgtggtcg cggccgaggt ctgtcctaca gtcctcagga ctctactccc tcagcagcgt
 ggtgaccgtg ccctccagca acttcggcac ccagacctac acctgcaacg tagatcacaa
                                                                          60
 gcccagcaac accaaggtgg acaagagagt tgagcccaaa tcttgtgaca aaactcacac
                                                                         120
 atgcccaccg tgcccagcac ctgaactcct ggggggaccg tcagtcttcc tcttccccg
                                                                         180
 catcccctt ccaaacctgc ccgggcggcc gctcgaaagc cgaattccag cacactggcg
                                                                         240
 gccggtacta gtgganccna acttggnanc caacctggng gaantaatgg gcataanctg
                                                                         300
 tttctggggg gaaattggta tccngtttac aattcccnca caacatacga gccggaagca
                                                                         360
 taaaagngta aaagcctggg ggnggcctan tgaagtgaag ctaaactcac attaattngc
                                                                         420
 gttgccgctc actggcccgc ttttccagc
                                                                         480
                                                                        509
       <210> 286
       <211> 336
       <212> DNA
       <213> Homo sapien
       <220>
      <221> misc_feature
      <222> (1)...(336)
      <223> n = A, T, C or G
      <400> 286
tcgagcggcc gcccgggcag gtttggaagg gggatgcggg ggaagaggaa gactgacggt
cccccagga gttcaggtgc tgggcacggt gggcatgtgt gagttttgtc acaagatttg
                                                                         60
ggctcaactc tcttgtccac cttggtgttg ctgggcttgt gatctacgtt gcaggtgtag
                                                                        120
gtctgggngc cgaagttgct ggagggcacg gtcaccacgc tgctgaggga gtagagtcct
                                                                        180
gaggactgta ngacagacct cggccgngac cacgctaagc cgaattctgc agatatccat
                                                                        240
                                                                        300
cacactggcg gccgctccga gcatgcattt tagagg
                                                                        336
      <210> 287
      <211> 30
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(30)
      <223> n = A, T, C or G
      <400> 287
agcgtggncg cggacganga caacaaccc
                                                                        30
      <210> 288
      <211> 316
      <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1) ... (316)
     \langle 223 \rangle n = A,T,C or G
```

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```
<400> 288
tegageggee geeegggeag gneeacateg geagggtegg ageeetggee geeatacteg
                                                                         60
aactggaatc catcggtcat gctcttgccg aaccagacat gcctcttgtc cttggggttc
                                                                        120
ttgctgatgn accagttctt ctgggccaca ctgggctgag tggggtacac gcaggtctca
                                                                        180
ccagtctcca tgttgcagaa gactttgatg gcatccaggt tgcagccttg gttggggtca
                                                                        240
atccagtact ctccactctt ccagtcagag tggcacatct tgaggtcacg gcaggtgcgg
                                                                        300
gcggggttct tgacct
                                                                        316
      <210> 289
      <211> 308
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(308)
      <223> n = A, T, C or G
      <400> 289
agcgtggtcg cggccgaggt ccagcctgga gataanggtg aaggtggtgc ccccggactt
                                                                         60
ccaggtatag ctggacctcg tggtagccct ggtgagagag gtgaaactgg ccctccagga
                                                                        120
cctgctggtt tccctggtgc tcctggacag aatggtgaac ctggnggtaa aggagaaaga
                                                                        180
ggggctccgg ntganaaagg tgaaggaggc cctcctgnat tggcaggggc cccangactt
                                                                        240
agaggtggag ctggcccccc tggccccgaa ggaggaaagg gtgctgctgg tcctcctggg
                                                                        300
ccacctgg
                                                                        308
      <210> 290
      <211> 324
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (324)
      <223> n = A, T, C or G
      <400> 290
tcgagcggcc gcccgggcag gtctgggcca ggaggaccaa taggaccagt aggaccctt
                                                                         60
gggccatctt tccctgggac accatcagca cctggaccgc ctggttcacc cttgtcaccc
                                                                        120
tttggaccag gacttccaag acctcctctt tctccaggca ttccttgcag accaggagta
                                                                        180
ccancagcac caggtggccc aggaggacca gcagcaccct ttcctccttc gggaccaggg
                                                                        240
ggaccagete cacetetaag teetggggee cetgecaate caggagggee teetteacet
                                                                        300
ttctcacccg gagcccctct ttct
                                                                        324
      <210> 291
      <211> 278
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(278)
      \langle 223 \rangle n = A, T, C or G
```

```
<400> 291
 tcgagcggcc gcccgggcag gtccaccggg atattcgggg gtctggcagg aatgggaggc
 atccagaacg agaaggagac catgcaaagc ctgaacgacc gcctggcctc ttacctggac
                                                                         60
 agagtgagga gcctggagac cgacaaccgg aggctggaga gcaaaatccg ggagcacttg
                                                                        120
 gagaagaagg gaccccaggt cagagactgg agccattact tcaagatcat cgaggacctg
                                                                        180
 agggeteana tettegeaaa tactgengae aatgeeeg
                                                                        240
                                                                        278
       <210> 292
       <211> 299
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(299)
       \langle 223 \rangle n = A,T,C or G
       <400> 292
 atgcgnggtc gcggccgang accanctctg gctcatactt gactctaaag ncntcaccag
 nanttacggn cattgccaat ctgcagaacg atgcgggcat tgtccgcant atttgcgaag
                                                                         60
 atctgagece teaggneete gatgatettg aagtaangge teeagtetet gacetggggt
                                                                        120
 cccttcttct ccaagtgctc ccggattttg ctctccagcc tccggttctc ggtctccaag
                                                                        180
ncttctcact ctgtccagga aaagaggcca ggcggncgat cagggctttt gcatggact
                                                                        240
                                                                        299
       <210> 293
       <211> 101
       <212> DNA
       <213> Homo sapien
       <400> 293
agcgtggtcg cggccgaggt tgtacaagct ttttttttt tttttttt tttttttt
                                                                        60
ttttttttt tttttttt ttttttt ttttttt t
                                                                       101
      <210> 294
      <211> 285
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(285)
      <223> n = A, T, C or G
      <400> 294
togagoggoo gooogggoag gtotgocaac accaagattg gooocogoog catcoacaca
gttngtgtgc ggggaggtaa caagaaatac cgtgccctga ggntggacgn ggggaatttc
                                                                        60
tcctggggct cagagtgttg tactcgtaaa acaaggatca tcgatgttgt ctacaatgca
                                                                       120
tctaataacg agctggttcg taccaagacc ctggtgaaga attgcatcgt gctcatngac
                                                                       180
                                                                       240
agcacaccgt accgacagtg ggtaccgaag tcccactatg cncct
                                                                       285
      <210> 295
      <211> 216
      <212> DNA
      <213> Homo sapien
```

```
<400> 295
tcgagcggcc gcccgggcag gtccaccaca cccaattcct tgctggtatc atggcagccg
                                                                        60
ccacgtgcca ggattaccgg ctacatcatc aagtatgaga agcctgggtc tcctcccaga
                                                                       120
qaaqtqqtcc ctcgqccccq ccctgqtqtc acaqaqqcta ctattactqq cctqqaaccq
                                                                       180
ggaaccgaat atacaattta tgtcattgcc ctgaag
                                                                       216
      <210> 296
      <211> 414
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(414)
      <223> n = A, T, C or G
      <400> 296
                                                                        60
agcqtqntcn cggccgagga tggggaagct cgnctgtctt tttccttcca atcaggggct
                                                                       120
nnntcttctg attattcttc agggcaanga cataaattgt atattcggnt cccggttcca
qnccagtaat agtagcctct gtgacaccag ggcggggccg agggaccact tctctgggag
                                                                       180
                                                                       240
qaqacccaqq cttctcatac ttgatgatga agccggtaat cctggcacgt gggcggctgc
                                                                       300
catgatacca ccaangaatt gggtgtggtg gacctgcccg ggcgggccgc tcgaaaancc
gaattentge aagaatatee atcacaettg ggegggeegn tegaaceatg catentaaaa
                                                                       360
gggccccaat ttccccccta ttaggngaag ccncatttaa caaattccac ttgg
                                                                       414
      <210> 297
      <211> 376
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(376)
      <223> n = A, T, C or G
      <400> 297
                                                                        60
tegagegge georgggeag gtetegeggt egeactggtg atgetggtee tgttggtee
                                                                       120
cccggcctc ctggacctcc tggtccccct ggtcctccca gcgctggttt cgacttcagc
                                                                       180
ttcctqcccc agccacctca agagaaggct cacgatggtg gccgctacta ccgggctgat
                                                                       240
qatqccaatq tqqttcqtga ccgtgacctc gaggtggaca ccaccctcaa gagccttgag
                                                                        300
ccagcagaat cgaaaacatt cggaacccaa gaaqqqcaaq cccqcaaaqa aaccccgccc
                                                                        360
qcacctqqcc qnqaacctcc aagaangtgc ccacntcttg actgggaaaa aaagggaaaa
                                                                        376
ntacttggaa ttggac
      <210> 298
      <211> 357
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(357)
      <223> n = A, T, C or G
      <400> 298
```

```
agcgtggtcg cggccgaggt ccacatcggc agggtcggag ccctggccgc catactcgaa
 ctggaatcca tcggtcatgc tctcgccgaa ccagacatgc ctcttgtcct tggggttctt
                                                                         60
 gctgatgtac cagttettet gggccacact gggctgagtg gggtacacgc aggtetcacc
                                                                        120
 agtetecatg ttgcagaaga etttgatgge atccaggttg cagcettggt tggggtcaat
                                                                        180
                                                                        240
 ccagtactct ccactcttcc agtcagaagt ggcacatctt gaggtcacgg cagggtgcgg
                                                                        300
 geggggttet tgegggetge cettetggge teeeggaatg ttetnngaac ttgetgg
                                                                        357
       <210> 299
       <211> 307
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(307)
       <223> n = A, T, C or G
       <400> 299
agegtggteg eggeegaggt ceaetagagg tetgtgtgee attgeecagg cagagtetet
                                                                        60
gcgttacaaa ctcctaggag ggcttgctgt gcggagggcc tgctatggtg tgctgcggtt
                                                                        120
catcatggag agtggggcca aaggctgcga ggttgtggtg tctgggaaac tccgaggaca
                                                                       180
gagggctaaa tccatgaagt ttgtggatgg cctgatgatc cacagcggag accctgttaa
                                                                       240
ctactacgtt gacacttgct tgtgcgccac gtgttgctca nacangggtg ggctgggcat
                                                                       300
caaggng
                                                                       307
      <210> 300
      <211> 351
      <212> DNA
      <213> Homo sapien
      <400> 300
tegageggee geeegggeag gtetgeeaag gagaeeetgt tatgetgtgg ggaetggetg
                                                                        60
gggcatggca ggcggctctg gcttcccacc cttctgttct gagatggggg tggtgggcag
                                                                       120
tateteatet ttgggtteca caatgeteae gtggteagge aggggettet tagggeeaat
                                                                       180
cttaccagtt gggtcccagg gcagcatgat cttcaccttg atgcccagca caccctgtct
                                                                       240
gagcaacacg tggcgcacag caagtgtcaa cgtaagtaag ttaacagggt ctccgctgtg
                                                                       300
gatcatcagg ccatccacaa acttcatgga tttaaccctc tgtcctcgga q
                                                                       351
      <210> 301
      <211> 330
      <212> DNA
      <213> Homo sapien
      <400> 301
tegageggee geeegggeag gtgttteaga ggtteeaagg teeactgtgg aggteeeagg
                                                                        60
agtgctggtg gtgggcacag aggtccgatg ggtgaaacca ttgacataga gactgttcct
                                                                       120
gtccagggtg taggggccca gctctttgat gccattggcc agttggctca gctcccagta
                                                                       180
cagcegetet etgitgagte cagggetett ggggteaaga tgatggatge agatggeate
                                                                       240
cactecagtg getgetecat cettetegga eetgagagag gteagtetge agecagagta
                                                                       300
cagagggcca acactggtgt tctttgaata
                                                                       330
      <210> 302
      <211> 317
      <212> DNA
      <213> Homo sapien
```

```
<220>
      <221> misc_feature
      <222> (1)...(317)
      <223> n = A, T, C or G
agcgtggtcg cggccgaggt ctgtactggg agctaagcaa actgaccaat gacattgaag
                                                                        60
agctgggccc ctacaccctg gacaggaaca gtctctatgt caatggtttc acccatcaga
                                                                       120
getetgtgne caccaccage actectggga cetecacagt ggattteaga aceteaggga
                                                                       180
ctccatcctc cctctccagc cccacaatta tggctgctgg ccctctcctg gtaccattca
                                                                       240
ccctcaactt caccatcacc aacctgcagt atggggagga catgggtcac cctgnctcca
                                                                       300
ggaagttcaa caccaca
                                                                       317
      <210> 303
      <211> 283
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(283)
      <223> n = A, T, C or G
      <400> 303
tegageggee geeeggaeag gtetgggegg atageaeegg geatattttg gaatggatga
                                                                        60
ggtctggcac cctgagcagt ccagcgagga cttggtctta gttgagcaat ttggctagga
                                                                       120
ggatagtatg cagcacggnt ctgagnctgt gggatagctg ccatgaagta acctgaagga
                                                                       180
ggtgctggct ggtangggtt gattacaggg ttgggaacag ctcqtacact tqccattctc
                                                                       240
tgcatatact ggttagtgag gtgagcctgg ccctcttctt ttg
                                                                       283
      <210> 304
      <211> 72
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(72)
      <223> n = A, T, C or G
      <400> 304
agcgtggtcg cggccgaggt gagccacagg tgaccggggc tgaagctggg gctgctggnc
                                                                        60
ctgctggtcc tg
                                                                        72
      <210> 305
      <211> 245
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(245)
      <223> n = A, T, C or G
```

```
<400> 305
   cagengetee naeggggeet gngggaccaa caacacegtt tteaccetta ggeeetttgg
   ctectette teetttagea ceaggttgae cageagence ancaggaeca geaaateeat
                                                                           60
   tggggccagc aggaccgacc tcaccacgtt caccagggct tccccgagga ccagcaggac
                                                                          120
   cagcaggace agcagececa gettegeece ggteacetgt ggeteacete ggeegegace
                                                                          180
                                                                          240
                                                                          245
         <210> 306
        <211> 246
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(246)
        <223> n = A, T, C or G
        <400> 306
  tegageggte geeegggeag gteeaceggg atageegggg gtetggeagg aatgggagge
 atccagaacg agaaggagac catgcaaagc ctgaacgacc gcctggcctc ttacctggac
                                                                          60
 agagtgagga gcctggagac cganaaccgg aggctggana gcaaaatccg ggagcacttg
                                                                         120
 gagaagaagg gaccccaggt caagagactg gagccattac ttcaagatca tcgagggacc
                                                                         180
                                                                         240
                                                                         246
        <210> 307
        <211> 333
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1) ... (333)
       <223> n = A, T, C \text{ or } G
       <400> 307
 agegnggteg eggeegaggt eeagetetgt eteataettg actetaaagt eateageage
 aagacgggca ttgtcaatct gcagaacgat gcgggcattg tccgcagtat ttgcgaagat
                                                                         60
ctgagccctc aggtcctcga tgatcttgaa gtaatggctc cagtctctga cctggggtcc
                                                                        120
cttettetee aagtgeteee ggattttget etceageete eggttetegg tetecagget
                                                                        180
cctcactctg tccaggtaag aaggcccagg cggtcgttca ggctttgcat ggtctccttc
                                                                        240
tcgttctgga tgcctcccat tcctgccaga ccc
                                                                        300
                                                                        333
      <210> 308
      <211> 310
      <212> DNA
      <213> Homo sapien
      <400> 308
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WO 00/36107 101 PCT/US99/30270

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Asn Leu Val Pro Arg Leu Pro Ala Leu Ser Trp Cys Tyr Ser Leu Ser
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Thr Ser Pro Ser Pro Thr Cys Gly Met Arg Arg Thr Cys Ser Thr Leu
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75

Leu Phe Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu

70

Thr	Leu	Leu	Arg 100	Pro	Glu	Lys	Asp	Gly 105	Thr	Ala	Thr	Gly	Val 110	Asp	Ala
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	Leu 130					135					140				
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	Arg			165					170					175	
	Leu		180					185					190		
	Ser	195					200					205			
	Arg 210					215					220				
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	Val			245					250					255	
	Lys		260					265					270		_
	Asp	275					280					285	_		
	Ser 290					295					300				
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	Thr			325					330					335	
	Thr		340					345					350		
	Leu	355					360					365			
	Leu 370					375					380			_	
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	Leu			405					410					415	
	Gln Gly		420					425					430		
	Glu	435					440					445		_	_
	450 Phe					455					460				
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	Asp			485		,			490					495	
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	Tyr	515					520					525			
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 Pro Thr Ser Ser Glu Tyr Ile Thr Leu Leu Arg Asp Ile Gln Asp Lys
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Tyr Gln Arg Asn Lys Arg Asn Ile Glu Asp Ala Leu Asn Gln Leu Phe
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Arg Asn Ser Ser Ile Lys Ser Tyr Phe Ser Asp Cys Gln Val Ser Thr
   770 775
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Phe Arg Ser Val Pro Asn Arg His His Thr Gly Val Asp Ser Leu Cys
785 790
                      795
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Glu Phe Leu Arg Met Thr Arg Asn Gly Thr Gln Leu Gln Asn Phe Thr
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      835 840
Glu Pro Leu Thr Gly Asn Ser Asp Leu Pro Phe Trp Ala Val Ile Leu
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Ile Gly Leu Ala Gly Leu Leu Gly Leu Ile Thr Cys Leu Ile Cys Gly
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<210> 326
<211> 455
<212> DNA
<213> Homo sapiens
<400> 326
tccgtgagga tgagcttcga gtccttcacc aggcactgca ggggcacagt cacgtcaatc 60
accttcacct tctcgctctt cctgctcttg tcattgacaa acttcccgta ccaggcattg 120
acgatgatga ggcccattct ggactcttct gcctcaatta tccttcggac agattcctgc 180
atcagecgga cageggacte egectettge ttettetgea geacateggt ggeggegett 240
tccctctgct tctccaattc cttctcttc tgagccctga ggtatggttt gatgatcaga 300
cggtgcatgg caaagtagac cactagaggc cccacggtgg catagaacat ggcgctgggc 360
agaagctggt ccgtcaagtg aatagggaag aagtatgtct gactggccct gttgagcttg 420
actttgagag aaacgccctg tggaactcca acgct
<210> 327
<211> 321
<212> DNA
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<213> Homo sapiens
<400> 327
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aagccaccct cttcccgcag catggtgaac aggaagttca taaggacggc gtgtttgcga 180
ggatatttct gacacagggc actgatggcc tggacaacca ccaccttgaa ttcatccgag 240
atttctgaca tgaaggagga gatctgcttc atgaggcggt cgatgctgct ctcgctgccc 300
gtcttaagga gggtggtgat g
<210> 328
<211> 476
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(476)
<223> n = A, T, C or G
<400> 328
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ccaagaggta atgcactcct tttcccatct ctccaccatc tgtatcctgg ccmagaaaaa 180
cttcccttca aaccaaccaa aatttccttt caaaggcata acccaaatgc catccttggt 240
coggtotaat aaagcotooc coattitto cotggtatgo attoccaggo tocctggoot 300
threagggett netgetetgt ggteatagtt tateterese caettgetgg gageteettg 360
aaggcaaaga ctctactgcc tccatctatc cagtggaagt ggctcttcag agggtgccaa 420
gttagtatgt atgactgtca tctctcccaa cagggcctga cttggsaggg cttcca
<210> 329
<211> 340
<212> DNA
<213> Homo sapiens
<400> 329
cgagggagat tgccagcacc ctgatggaga gtgagatgat ggagatcttg tcagtgctag 60
ctaagggtga ccacagccct gtcacaaggg ctgctgcagc ctgcctggac aaagcagtgq 120
aatatgggct tatccaaccc aaccaagatg gagagtgagg gggttgtccc tgggcccaag 180
gctcatgcac acgctaccta ttgtggcacg gagagtaagg acggaagcag ctttggctgg 240
tggtggctgg catgcccaat actcttgccc atcctcgctt gctgccctag gatgtcctct 300
gttctgagtc agcggccacg ttcagtcaca cagccctgct
                                                                   340
<210> 330
<211> 277
<212> DNA
<213> Homo sapiens
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caggatgcag ccagtgctga cattgttgag gtgcaggagc tctactccat taagggagaa 120
ggccaggcca aaaaggttgt tggcaatcca gtgcttcctc agcaggtacc aqacqccaac 180
gatgctgctc aggcccaggc acaccaggtc cttggtgtca aattcataat tgatgatctc 240
ctccttgttt tcccagaacc ctgtgtgaag agcagac
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 <211> 136
 <212> DNA
 <213> Homo sapiens
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 atacaaacca cacacacaat gaggatgaaa acagataaca ggtaaaatga cctcacctgc 120
 ccgggcggcc gctcga
                                                                    136
 <210> 332
 <211> 184
 <212> DNA
 <213> Homo sapiens
 <400> 332
ttgtgagata aacgcagata ctgcaatgca ttaaaacgct tgaaatactc atcagggatg 60
ttgctgatct tattgttgtc taagtagaga gttagaagag agacagggag accagaaggc 120
agtctggcta tctgattgaa gctcaagtca aggtattcga gtgatttaag acctttaaaa 180
 gcag
                                                                    184
 <210> 333
 <211> 384
<212> DNA
<213> Homo sapiens
<400> 333
cggaaaactt cgaggaattg ctcaaagtgc tgggggtgaa tgtgatgctg aggaagattg 60
ctgtggctgc agcgtccaag ccagcagtgg agatcaaaca ggagggagac actttctaca 120
tcaaaacctc caccacgtg cgcaccacag agattaactt caaggttggg gaggagtttg 180
aggagcagac tgtggatggg aggccctgta agagcctggt gaaatgggag agtgagaata 240
aaatggtetg tgagcagaag eteetgaagg gagagggeee caagaceteg tggaccagag 300
aactgaccaa cgatggggaa ctgatcctga ccatgacggc ggatgacgtt gtgtgcacca 360
gggtctacgt ccgagagtga gcgg
                                                                   384
<210> 334
<211> 169
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(169)
<223> n = A, T, C or G
<400> 334
cnacaaacag agcagacacc ctggatccgg tcctgctact ggccaggacg gctggaccgt 60
aaaattgaat ttccacttcc tgaccgccgc cagaagagat tgattttctc cactatcact 120
agcaagatga acctctctga ggaggttgac ttggaagact atgtngccc
<210> 335
<211> 185
<212> DNA
<213> Homo sapiens
```

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<400> 335
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tgctgactga tggtgctgtg acggatgtgg aagccacacg tgaggctgtg gtgcgtgcct 120
cgaacctgcc catgtcagtg atcattgtgg gtgtgggtgg tgctgacttt gaggccatgg 180
agcag
<210> 336
<211> 358
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(358)
<223> n = A, T, C or G
<400> 336
ctgcccctgc cttacggcgg ccaganacac acccaggatg gcattggccc caaacttgga 60
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agagagacct gagctgatga gggctggcgc gatggtggag ttgatgtggt ccactgcctt 180
caggacacct ttgcctaagt aacgetgttt gtctccatcc ctcagctcca gggcctcata 240
gatgcccgta gaggctccac tgggcactgc agcccggaaa agacctttgg cagtatagag 300
atocacctoc actgtggggt tcccgcggga gtccaggate tcccgggccc agatette
<210> 337
<211> 271
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(271)
<223> n = A, T, C or G
<400> 337
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gaaatcctgc ccagcatggg attcagaacc tggtctgcaa ccaaatccac cgtcaaagtt 120
catacaggat aaaacaaatt caattgcctt ttccacatta atagcatcaa gcttccccaa 180
caaagccaaa gttgccaccg cacaaaaaga gaatcttgtg tcaatttctc cctactttat 240
aaaaqtagat ttttcacatc ccatgaagca g
                                                                   271
<210> 338
<211> 326
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(326)
<223> n = A, T, C \text{ or } G
<400> 338
ctgtgctccc gactngnnca tctcaggtac caccgactgc actgggcqqq gccctctgqg 60
gggaaaggct ccacggggca gggatacatc tcgaggccag tcatcctctg gaggcagccc 120
aatcaggtca aagattttgc ccaactggtc ggcttcagag tttccacaga agagaggctt 180
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tegacgaaac atetetgeaa agatacagee aacaeteeac atgteeacag gtgttgeata 240
  tgtggactgc agaagaactt cgggagctcg gtaccagagt gtaacaacca cgggtgtaag 300
  tgccatctgg tagctgtaga ttctgg
  <210> 339
  <211> 260
  <212> DNA
  <213> Homo sapiens
  <220>
 <221> misc_feature
 <222> (1)...(260)
 <223> n = A, T, C or G
 <400> 339
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 caaggacgnc acatttccac ttgcgaatgn nctcanggct catcttgaag aanaagnanc 120
 ccaagtgctg gatcccagac tcgggggtaa ccttgtgggt aagagctcat ccagtttatg 180
 ctttaggacg tccanctact cgggggagct ggaagcctgc gtggatgcgg ccctgctgga 240
 cctcggccgc gaccacgcta
 <210> 340
 <211> 220
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(220)
 <223> n = A, T, C or G
 <400> 340
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gcagtagcgg tagcggcact cgtctatgtc cacacactcg ggcccgatct tgcggtaacc 120
atcagggcag gtgcactgat aggagccagg caagttatgg cagtcctggc tggggcgaca 180
gtcgtgcagg gcctgggcac actcgtccac atccacacag
<210> 341
<211> 384
<212> DNA
<213> Homo sapiens
<400> 341
ctgctaccag gggagcgaga gctgactatc ccagcctcgg ctaatgtatt ctacgccatg 60
gatggagett cacacgattt ceteetgegg cageggegaa ggteetetae tgetacaceg 120
ggcgtcacca gtggcccgtc tgcctcagga actcctccga gtgagggagg agggggctcc 180
tttcccagga tcaaggccac agggaggaag attgcacggg cactgttctg aggaggaagc 240
cccgttggct tacagaagtc atggtgttca taccagatgt gggtagccat cctgaatggt 300
ggcaattata tcacattgag acagaaattc agaaagggag ccagccaccc tggggcagtg 360
aagtgccact ggtttaccag acag
<210> 342
<211> 245
<212> DNA
<213> Homo sapiens
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tgtaaccaac aagaatgacc ccaagtccat caactctcga gtcttcattg gaaacctcaa 120
cacagetetg gtgaagaaat cagatgtgga gaccatette tetaagtatg geegtgtgge 180
eggetgttet gtgcacaagg getatgeett tgtteagtae tecaatgage gecatgeeeg 240
ggcag
<210> 343
<211> 611
<212> DNA
<213> Homo sapiens
<400> 343
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tctcagccat ctttgaagct tgaaagaaga gtctttggta ttttgtaaac gttagcagac 120
tttcctgcca gtgtcagaaa atcctatta tgaatcctgt cggtattcct tggtatctga 180
aaaaaatacc aaatagtacc atacatgagt tatttctaag tttgaaaaat aaaaagaaat 240
tgcatcacac taattacaaa atacaagtto tggaaaaaat attttctto attttaaaac 300
tttttttaac taataatggc tttgaaagaa gaggcttaat ttgggggtgg taactaaaat 360
caaaagaaat gattgacttg agggtctctg tttggtaaga atacatcatt agcttaaata 420
agcagcagaa ggttagtttt aattatgtag cttctgttaa tattaagtgt tttttgtctg 480
ttttacctca atttgaacag ataagtttgc ctgcatgctg gacatgcctc agaaccatga 540
atagcccgta ctagatcttg ggaacatgga tcttagagtc ctttggaata agttcttata 600
taaatacccc c
                                                                   611
<210> 344
<211> 311
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(311)
<223> n = A, T, C or G
<400> 344
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aagaagtatt cagaaaagag atgtcccagt tcatcgtcca gtgcctgaac ccttaccgga 120
aacctgactg caaagtggga agaattacca caactgaaga ctttaaacat ctggctcgca 180
agetgaetea eggtgttatg aataaggage tgaagtaetg taagaateet gaggaeetgg 240
agtgcaatga gaatgtgaaa cacaaaacca aggantacat taanaagtac atgcannaan 300
tttggggctt g
                                                                   311
<210> 345
<211> 201
<212> DNA
<213> Homo sapiens
<400> 345
cacacggtca tecegactge caacetggag geecaggeec tgtggaagga geegggeage 60
aatgtcacca tgagtgtgga tgctgagtgt gtgcccatgg tcagggacct tctcaggtac 120
ttctactccc gaaggattga catcaccctg tcgtcagtca agtgcttcca caagctggcc 180
tctgcctatg gggccaggca g
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  <211> 370
  <212> DNA
  <213> Homo sapiens
  <400> 346
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 tetetteaga atgttetgga geageagttt gaggegggtg atgegttgga agggeagaat 120
 cagaaaggac ttgagggaaa ggcgctggca gacggggtcg ctctccagct tctccaagac 180
 ctcccggaaa ttgctgttgc tattcatcag gctctggaag gtgcgttcct gataggtctg 240
 gttggtgaca taaggcaggt agacccggcg gaagtctggg gcgtggttca ggactacgtc 300
 acatacttgg aaggagaaga tattgttctc aaagttctct tecaggtctg aaaggaacgt 360
 <210> 347
 <211> 416
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(416)
 <223> n = A, T, C or G
 <400> 347
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 ccccatttga acaagcaaag aaggtgataa ccatgtttgt acagcgacag gtgtttgctg 120
 agaacaagga tgagattgct ttagtcctgt ttggtacaga tggcactgac aatccccttt 180
 ctggtgggga tcagtatcag aacatcacag tgcacagaca tctgatgcta ccagattttg 240
 atttgctgga ggacattgaa agcaaaatcc aaccaggttc tcaacaggct gacttcctgg 300
 atgcactaat cgtgagcatg gatgtgattc aacatgaaac aataggaaag aagtttggag 360
aagaggcata ttgaaatatt cactgacctc aagcagcccg attcagcaaa agtcan
 <210> 348
<211> 351
<212> DNA
<213> Homo sapiens
<400> 348
gtacaggaga ggatggcagg tgcagagcgg gcactgagct ctgcaggtga aagggctcgg 60
cagttggatg ctctcctgga ggctctgaaa ttgaaacggg caggaaatag tctggcagcc 120
tetacageag aagaaaegge aggeagtgee cagggaegag caggagaeag atgeetteet 180
cttgtctcaa ctgcaaagag gcgttccttc ctctttcact aatcetcctc agcacagacc 240
ctttacgggt gtcaggctgg gggacagtaa ggtctttccc ttcccacaag gccatatctc 300
aggetgtete agtgggggga aacettggae aataceeggg etttettggg e
<210> 349
<211> 207
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (207)
<223> n = A, T, C or G
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nccgggacat ctccaccctc aacagtggca agaagagcct ggagactgaa cacaaggcct 60
tgaccagtga gattgcactg ctgcagtcca ggctgaagac agagggctct gatctgtgcg 120
acagagtgag cgaaatgcag aagctggatg cacaggtcaa ggagctggtg ctgaagtcgg 180
cggtggaggc tgagcgcctg gtggctg
<210> 350
<211> 323
<212> DNA
<213> Homo sapiens
<400> 350
ccatacaggg ctgttgccca ggccctagag gtcattcctc gtaccctgat ccagaactgt 60
ggggccagca ccatccgtct acttacctcc cttcgggcca agcacaccca ggagaactgt 120
gagacctggg gtgtaaatgg tgagacgggt actttggtgg acatgaagga actgggcata 180
tgggagccat tggctgtgaa gctgcagact tataagacag cagtggagac ggcagttctg 240
ctactgcgaa ttgatgacat cgtttcaggc cacgaaaaga aaggcgatga ccagagccgg 300
caaggcgggg ctcctgatgc tgg
<210> 351
<211> 353
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(353)
\langle 223 \rangle n = A,T,C or G
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tgtttttgtt ttgtagggtt tttttccttc tccacctctc cctgtctctt ttgctccatg 120
ttgtccgttt ctgtggggtt aggtttatgt ttttaatcat ctgaggtcac gtctatttcc 180
teeggacteg cetgettggt ggcgattete caeeggttaa tatggtgegt ceettttte 240
ttttgttgcg aatctgagcc ttcttcctcc agettctgcc ttttgaactt tgttcttcgg 300
ttctgaaacc atacttttac ctgagtttcc gtgaggctga ggctgtgtgc caa
<210> 352
<211> 467
<212> DNA
<213> Homo sapiens
<400> 352
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aatttgagca gaacctgtct gagaaactct ctgaacaaga attacaattt cgtcgtctca 120
gtcaagagca agttgacaac tttactctgg atataaatac tgcctatgcc agactcagag 180
gaatcgaaca ggctgttcag agccatgcag ttgctgaaga ggaagccaga aaagcccacc 240
aactctggct ttcagtggag gcattaaagt acagcatgaa gacctcatct gcagaaacac 300
ctactatccc gctgggtagt gcagttgagg ccatcaaagc caactgttct gataatgaat 360
tcacccaage tttaaccgca gctatccctc cagagtccct gacccgtggg gtgtacagtg 420
aagagaccct tagagcccgt ttctatgctg ttcaaaaact ggcccqa
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<210> 353
<211> 350
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<212> DNA
 <213> Homo sapiens
 <400> 353
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 gaaatetgte cecaccagga acageeeetg gaaaacggee eegteeteta ceacettgtg 120
 gaaatgetge acgggaactg cetectggag gaccagettt acetteecca gacatttgte 180
 ctgattgtgt agttttcctg gactgcattt caaattgact caggaactgt ttattgcatg 240
 gagttacaac aggattetga ceatgaagtt etettttagg taacagatee attaactttt 300
 ttgaagatgc ttcagatcca acaccaacaa gggcaaaccc ctttgactgg
 <210> 354
 <211> 351
 <212> DNA
 <213> Homo sapiens
 <400> 354
 atttagatga gatctgaggc atggagacat ggagacagta tacagactcc tagatttaag 60
 ttttaggttt tttgcttttc taatcaccaa ttcttatata caatgtatat tttagactcg 120
agcagatgat catcttcatc ttaagtcatt ccttttgact gagtatggca ggattagagg 180
gaatggcagt atagatcaat gtcttttct gtaaagtata ggaaaaacca gagaggaaaa 240
aaagagctga caattggaag gtagtagaaa attgacgata atttcttctt aacaaataat 300
agttgtatat acaaggaggc tagtcaacca gattttattt gttgagggcg a
 <210> 355
 <211> 308
 <212> DNA
<213> Homo sapiens
<400> 355
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atgcaaatgt tgatgaggtg gaattgaagc cagatacctt aataaaatta tatcttggtt 120
ataaaaataa gaaattaagg gttaacatca atgtgccaat gaaaaccgaa cagaagcagg 180
aacaagaaac cacacaaa aacatcgagg aagaccgcaa actactgatt caggcggcca 240
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tcactcag
<210> 356
<211> 207
<212> DNA
<213> Homo sapiens
<400> 356
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atgaagaata ctgcaccgcc aacgcagtca ctgggccttg ccgtgcatcc ttcccacgct 120
ggtactttga cgtggagagg aactcctgca ataacttcat ctatggaggc tgccggggca 180
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<210> 357
<211> 188
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
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<222> (1)...(188)
<223> n = A, T, C or G
<400> 357
togaccacgo cotogtagog catgngotho aggacgatgo toagagtgat gaacaccocg 60
gtgcggccca cgccagcact gcagtgcacc gtgataggcc catcctgtcc aaactgctcc 120
ttggtcttat gcacctgccc gatgaagtca atgaatccct cgcctgtctt gggcacgccc 180
tgctctgg
<210> 358
<211> 291
<212> DNA
<213> Homo sapiens
<400> 358
ctgggagcat cggcaagcta ctgccttaaa atccgatctc cccgagtgca caatttctgt 60
cccttttaag ggttcacaac actaaagatt tcacatgaaa gggttgtgat tgatttgagc 120
aggcaggcgg tacgtgacag gggctgcatg caccggtggt cagagagaaa cagaacaggg 180
cagggaattt cacaatgttc ttctatacaa tggctggaat ctatgaataa catcagtttc 240
taagttatgg gttgattttt aactactggg tttaggccag gcaggcccag g
<210> 359
<211> 117
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(117)
<223> n = A, T, C or G
<400> 359
cccaaaaaaa ctcaaaaang taatgaatga tacccaangn gccttttcta gaaaaag
<210> 360
<211> 394
<212> DNA
<213> Homo sapiens
<400> 360
ctgttcctct ggggtggtcc agttctagag tgggagaaag ggagtcaggc gcattgggaa 60
togtggttoc agtotggttg cagaatotgo acatttgoca agaaatttto cotgtttgga 120
aagtttgccc cagetttccc gggcacacca cettttgtcc caagtgtctg ceggtegace 180
aatctgcctg ccacacattg accaagccag acccggttca cccagctcga ggatcccagg 240
ttgaagagtg gccccttgag gccctggaaa gaccaatcac tggacttctt cccttgagag 300
tcagaggtca cccgtgattc tgcctgcacc ttatcattga tctgcagtga tttctgcaaa 360
tcaagagaaa ctctgcaggg cactcccctg tttc
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<210> 361
<211> 394
<212> DNA
<213> Homo sapiens
<220>
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<221> misc_feature
  <222> (1)...(394)
  <223> n = A, T, C or G
  <400> 361
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  tgagtctgtg ggatagctgc catgaagtaa cctgaaggag gtgctggctg gtaggggttg 180
 attacagggt tgggaacagc tcgtacactt gccattctct gcatatactg gttagtgagg 240
 tgagcctggc gctcttcttt gcgctgagct aaagctacat acaatggctt tgtggacctc 300
 ggccgcgacc acgctaagcc gaattccagc acactggcgg ccgttactag tggatccgag 360
  ctcggtacca agcttggcgt aatcatggtc atag
 <210> 362
 <211> 268
 <212> DNA
 <213> Homo sapiens
 <400> 362
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 tgtttaagga tggtctcggt ggttaggccc actagaataa actgagtcca atacctctac 180
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 caaacttcaa tggttatgcg gggatgtt
 <210> 363
 <211> 323
 <212> DNA
 <213> Homo sapiens
 <400> 363
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 gacagacact ggcaacattg cggacaccct ccaggaagcg agaatgcaga gttteetetg 180
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<210> 364
<211> 393
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(393)
<223> n = A, T, C or G
<400> 364
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cacccagggg cactggcatc gtctccgcac ctgtgcctaa gaagctgctc atgatggctg 180
gcatcgatga ctgctacacc tcagcccggg gctgcactgc caccctgggc aacttcgcca 240
aggccacctt tgatgccatt tctaagacct acagctacct gacccccgac ctctggaagg 300
agactgtatt caccaagtct ccctatcagg agttcactga ccacctcgtc aagacccaca 360
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ccagagtctc cgtgcagcgg actcaggctc cag
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<211> 371
<212> DNA
<213> Homo sapiens
<400> 365
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aggagtteet etecaegtea aagtaeeage gtgggaagga tgeaeggeaa ggeeeagtga 120
ctgcgttggc ggtgcagtat tcttcatagt tgaacatatc gctggagtgg tcttcagaat 180
cctgccttct gggagcactt gggacagagg aatccgctgc attcctgctg gtggacctcq 240
gccgcgacca cgctaagccg aattccagca cactggcggc cgttactagt ggatccgagc 300
tcggtaccaa gcttggcgta atcatggtca tagctgtttc ctgtgtgaaa ttgttatccg 360
ctcacaattc c
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<210> 366
<211> 393
<212> DNA
<213> Homo sapiens
<400> 366
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<210> 367
<211> 327
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(327)
<223> n = A, T, C or G
<400> 367
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tgatcttgaa gtaatggctc cagtctctga cctggggtcc cttcttctcc aagtgctccc 180
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aggccaggcg gtcgttcagg ctttgcatgg tctccttctc gttctggatg cctcccattc 300
ctgccagacc cccggctatc ccggtgg
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<210> 368
<211> 306
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
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<222> (1)...(306)
 <223> n = A, T, C or G
 <400> 368
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 aacggaggca ctgtggccga gaagctggac tgggcccgcg agaggcttga gcagcaggta 180
 cctgtgaacc aagtgtttgg gcaggatgag atgatcgacg tcatcggggt gaccaagggc 240
 aaaggctaca aaggggtcac cagtcgttgg cacaccaaga agctgccccg caagacccac 300
 cgagga
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 <210> 369
 <211> 394
 <212> DNA
 <213> Homo sapiens
 <400> 369
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eggetgeeac gaaagtgegt ttetttgtgt tetegggttg gaacegtgat ttecacagae 120
cettgaaata cactgegttg acgaggacca gtctggtgag cacaccatca ataagatctg 180
gggacagcag attgtcaatc atatccctgg tttcattttt aacccatgca ttgatggaat 240
cacaggcaga ggctggatcc tcaaagttca cattccggac ctcacactgg aacacatctt 300
tgttccttgt aacaaaaggc acttcaattt cagaggcatt cttaacaaac acggcgttag 360
ccactgtcac aatgtcttta ttcttcttgg agac
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<210> 370
<211> 653
<212> DNA
<213> Homo sapiens
<400> 370
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acatcatcaa gtatgagaag cctgggtctc ctcccagaga agtggtccct cggccccgcc 120
ctggtgtcac agaggctact attactggcc tggaaccggg aaccgaatat acaatttatg 180
tcattgccct gaagaataat cagaagagg agcccctgat tggaaggaaa aagacagacg 240
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tteetteeae agtteaaaag acceettteg teacceaece tgggtatgae actggaaatg 360
gtattcagct tcctggcact tctggtcagc aacccagtgt tgggcaacaa atgatctttg 420
aggaacatgg ttttaggcgg accacaccgc ccacaacggc cacccccata aggcataggc 480
caagaccata cccgccgaat gtaggacaag aagctctctc tcagacaacc atctcatggg 540
ccccattcca ggacacttct gagtacatca tttcatgtca tcctgttggc actgatgaag 600
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<210> 371
<211> 268
<212> DNA
<213> Homo sapiens
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getecacetg gactacateg ggeettgeaa atacateece cettgeetgg actetgaget 180
gaccgaattc cccctgcgca tgcgggactg gctcaagaac gtcctggtca ccctgtatga 240
gagggatgag gacaacaacc ttctgact
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<211> 392
<212> DNA
<213> Homo sapiens
<400> 372
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cctggtgaga gaggtgaaac ctcggccgcg ac
<210> 373
<211> 388
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(388)
\langle 223 \rangle n = A, T, C or G
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aaccattggc ctgggccagc ttgcacgcct gaagagactc qqtcacqqaq ccaatctqqt 180
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ggttggtcac tgtgagatca tcccccacta cctggattcc tgcactggct gtgaacttct 300
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tgatgaagga cttgtacagg tcagccag
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<210> 374
<211> 393
<212> DNA
<213> Homo sapiens
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gcatcaaggt agacaagggc gtggtccccc tggcagggac aaatggcgag actaccaccc 180
aagggttgga tgggctgtct gagcgctgtg cccagtacaa gaaggacgga gctgacttcg 240
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aaaatgccaa tgttctggcc cgttatgcca gtatctgcca gcagaatggc attgtgccca 360
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<210> 375
<211> 394
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(394)
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<223> n = A, T, C or G
  <400> 375
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  aggaaagagg ggatgaactt gcagactctg cgcttgagat cttcaaacaa gcatcagcgt 120
  tttccagggc ttcccagagg tctgtgcgac tagcccctgt ctatcaaaag ttattagaga 180
  ggatgaagca ttagcttgaa gcactacagg aggaatgcac cacggcagct ctccgccaat 240
  ttctctcaga tttccacaga gactgtttga atgttttcaa aaccaagtat cacactttaa 300
  tgtacatggg ccgcaccata atgagatgtg agccttgtgc atgtggggga ggagggagag 360
  agatgtactt tttaaatcat gttcccccta aaca
 <210> 376
 <211> 392
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc feature
 <222> (1)...(392)
 <223> n = A, T, C or G
 <400> 376
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 gctccacctg gactacatcg ggccttgcaa atacatcccc ccttgcctgg actctgagct 180
 gaccgaattc cccctgcgca tgcgggactg gctcaagaac gtcctggtca ccctgtatga 240
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 <211> 292
 <212> DNA
 <213> Homo sapiens
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ctgccatatg gaggaggctc tggagtcctg ctctgtgtgg tccaggtcct ttccaccctg 180
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caagaagtgc cagttgatca atgaataaat aaacgagcct atttctcttt gc
<210> 378
<211> 395
<212> DNA
<213> Homo sapiens
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ctgctggaac tgctcctcca ggagactgct gattttggca ttcttttcc tttcatcata 360
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<211> 223
<212> DNA
<213> Homo sapiens
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agetecagee accaecagge tgageagtga ggagagaaag tttetgeetg geeetgeate 120
tggttccagc ccacctgccc tccccttttt cgggactctg tattccctct tgggctgacc 180
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<210> 380
<211> 317
<212> DNA
<213> Homo sapiens
<220>
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<222> (1)...(317)
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<400> 380
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attccgcagg ggccctcctc gccaaagaca gcctagagag gacggcaatg aagaagataa 180
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cttcaattac cgacgcagac gcccagaaaa ccctaaacca caagatggca aagagacaaa 300
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<210> 381
<211> 392
<212> DNA
<213> Homo sapiens
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<221> misc_feature
<222> (1)...(392)
<223> n = A, T, C or G
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<211> 234
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<213> Homo sapiens
<400> 382
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  cegegactic gttcaggtac atgaagaget ccaaggaggt ctggtgggtg gtgccatcet 180
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  <211> 396
  <212> DNA
  <213> Homo sapiens
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  <221> misc_feature
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  <223> n = A, T, C or G
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tetggetgea gactgaettt geteaggeet gaaaaggatg ggacageeac tggagtggat 480
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Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile Gly Glu Asp Gly Ile
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Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu Ser Asp Ile Val Ile 85 90 95

Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val His Glu Phe Lys Glu 100 105 105 105 110 110

Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met Phe Arg Gly Arg Thr 115 120 125

Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn Ala Ser Leu Arg Leu 130 135 140

Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr Lys Cys Tyr Ile Ile 145 150 155 160

Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu Tyr Lys Thr Gly Ala 165 170 170

Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn Ala Ser Ser Glu Thr 180 185 185 190

Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln Pro Thr Val Val Trp

Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser Glu Val Ser Asn Thr 210 215 215

Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met Lys Val Val Ser Val 230

Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser Cys Met Ile Glu Asn 255

Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val Thr Glu Ser Glu Ile 260

Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser Lys Ala Ser Leu Cys 275 280 285

Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu Leu Pro Leu Ser Pro 290 295 295 300

Tyr Leu Met Leu Lys 305

<210> 393

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<212> PRT

<213> Homo sapiens

# WO 00/36107 136 PCT/US99/30270

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Ile	Ile	Leu	Ala 20	Gly	Ala	Ile	Ala	Leu 25	Ile	Ile	Gly	Phe	Gly 30	Ile	Ser
Gly	Arg	His 35	Ser	Ile	Thr	Val	Thr 40	Thr	Val	Ala	Ser	Ala 45	Gly	Asn	Ile
Gly	Glu 50	Asp	Gly	Ile	Leu	Ser 55	Cys	Thr	Phe	Glu	Pro 60	Asp	Ile	Lys	Leu
Ser 65	Asp	Ile	Val	Ile	Gln 70	Trp	Leu	Lys	Glu	Gly 75	Val	Leu	Gly	Leu	Val 80
His	Glu	Phe	Lys	Glu 85	Gly	Lys	Asp	Glu	Leu 90	Ser	Glu	Gln	Asp	Glu 95	Met
Phe	Arg	Gly	Arg 100	Thr	Ala	Val	Phe	Ala 105	Asp	Gln	Val	Ile	Val 110	Gly	Asn
Ala	Ser	Leu 115	Arg	Leu	Lys	Asn	Val 120	Gln	Leu	Thr	Asp	Ala 125	Gly	Thr	Tyr
Lys	Cys 130	Tyr	Ile	Ile	Thr	Ser 135	Lys	Gly	Lys	Gly	Asn 140	Ala	Asn	Leu	Glu
Tyr 145	Lys	Thr	Gly	Ala	Phe 150	Ser	Met	Pro	Glu	Val 155	Asn	Val	Asp	Tyr	Asn 160
Ala	Ser	Ser	Glu	Thr 165	Leu	Arg	Cys	Glu	Ala 170	Pro	Arg	Trp	Phe	Pro 175	Gln
Pro	Thr	Val	Val 180	Trp	Ala	Ser	Gln	Val 185	Asp	Gln	Gly	Ala	Asn 190	Phe	Ser
Glu	Val	Ser 195	Asn	Thr	Ser	Phe	Glu 200	Leu	Asn	Ser	Glu	Asn 205	Val	Thr	Met
Lys	Val 210	Val	Ser	Val	Leu	Tyr 215	Asn	Val	Thr	Ile	Asn 220	Asn	Thr	Tyr	Ser
Cys 225	Met	Ile	Glu	Asn	Asp 230	Ile	Ala	Lys	Ala	Thr 235	Gly	Asp	Ile	Lys	Val 240
Thr	Glu	Ser	Glu	Ile 245	Lys	Arg	Arg	Ser	His 250	Leu	Gln	Leu	Leu	Asn 255	Ser
Lys	Ala	Ser	Leu 260	Cys	Val	Ser	Ser	Phe 265	Phe	Ala	Ile	Ser	Trp 270	Ala	Leu
Leu	Pro	Leu 275	Ser	Pro	Tyr	Leu	Met 280	Leu	Lys						

PCT/US99/30270

# 11729.1 contg

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# 11729-45.21.21.cons2

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# 11731.1contig

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## 11731.2contig

# 11734.1 contig

#### 11734.2contig

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### 11736.1 contg

## 11736.2contig

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### 11739-1&2

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# 11740.1.contig

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4 / 92

## 11766.1.contig

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## 11766.2.contig

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## 11773.2.contig

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#### 11775-132

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## 11777.1&2.cons

# 11779.2.contig

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AGCAGCTGGCCCGGGAGGCTGAAGCCCGGGCTGAACGTGAGGCCCGAGGCGCGAGACGG
GAGGAGCAGGAGGCTCGAGAGAAGGCCCAGGCTGAGCAGGAGCAGCAGCAGCGACTGCA
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## 11-31 & 37.cons

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## 11781-76-87-37

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## 11784182

## 11735.2.contig

#### 11718-1&2 cons

### 13690.4

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#### 13693.1

#### 13694.1

#### 13694.2

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#### 13695.1

#### 13695.2

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#### 13697.1

#### 13697.2

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### 13699.1&2

### 13703.3

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#### 13705.1

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## 13707.4

## 13708.1&2

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## 13709.1

# 137121&2

# 13714.1&2

# 13716.1&2

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#### 137223

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### 13722.4

# 13774-13698-13748

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### 13732.1

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# 13732.2

## 13735.2

### 13736.1

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AAATGGCATTCAGTGGGTACAAAGCC

## 13737.1&2

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## 13738.1

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AGFTA

#### 13738.2

## 13730.1&2

# 13741.1

### 14351.1

### 14351.2

ACCTTAAAGACATAGGAGAATTTATACTGGGAGAGAAAGCTTACAAATGTAAGGTTTCTG ACAAGACTTGGGAGTGATTCACACCTGGAACAACATACTGGACTTCACACTGGABAGAAA CCTTACAAGTGTAATGAGTGTGGCAAAGCCTTTGGCAAGCAGTCAACACTTATTCACCATC AGGCAATTCA

### 14354.2

AGTCAGGATCATGATGGCTCAGTTTCCCACAGCGATGAATGGAGGGCCAAATATGTGGGC
TATTACATCTGAAGAACGTACTAAGCATGATAAACAGTTTGATAACCTCAAACCTTCAGGA
GGTTACATAACAGGTGATCAAGCCCGTACTTTTTCCTACAGTCAGGTCTGCCGGCCCCGG
TTTTAGCTGAAATATGGGCCCTTATCAGATCTGAACAAGGATGGGAAGATGGACCAGCAAG
AGTTCTCTATAGCTATGAAACTCATCAAGTTAAAGTTGCAGGGCCAACAGCTGCCTGTAGT
CCTCCCTCCTATCATGAAACACCCCCTATGTTCTCTCCACTAATCTCTGCTCGTTTTGGGA
TGGGAAGCATGCCCAATCTGTCCATCATCAGCCATTGCCTCCAGTTGCACCTATAGCAAC
ACCCTTGTCTTCTGCTACTTCAGGGGACCAGTATTCCTCCCTTAATGATGCCTGCT

## 14354.1

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#### 16431.1.2

#### 16432-1

GACATGTTTGCCTGCAGGGGACCAGAGACAATGGGATTAGCCAGTGCTCACTGTTCTTTAT
GCTTCCAGAGAGGATGGGGACAGCTCTCAGGTCAGAATCCAGGCTGAGAAGGCCATGCTG
GTTGGGGGCCCCCGGAAGCACGGTCCGGATCCTCCCTGGCATCAGCGTAGACCCCGCTGC
AGGCTTGGGGTACCAAACTCATGCTCTGTACTGTTTTGGCCCCATGCGGTGAGAGCCCGCTCC
CTAGAAAAAGATTGGTCGTGCTAAGGAATCAGCTGCCCCCCTCATCCTCCGCATCCAATGCT
GGTGACAACATATTCCCTCTCCCAGGACACAGACTCGGTGACTCCACACTGGGCTGAGTGC
CCTCTGGAGGCTCGTGGCCTAAGGCAGCTCCGTAAGGCTGACTCCACACTGGGCTGAGTGG
GGTGAGGGTTTCTGACCCTTCGCTTCCCATCCATCCCATAACCGCTGAACTGGGTGAGTGG
GGTCA

### 16432.2

GATGGCATGGTCGTTGCTAATGTGCCTGCTGGGATGGAGCACTTCCTCCTGTGAGCCCAGG GGACCCGCTGTCCCTGGAGCTTGGGGCAAAGGAGGGAAGATGATACCAGGAAGGTGGG GCTGCAGCCAGGGGCCAGAGTCAGTTCAGGGAGTGTCCTCGGCCCTCAAAGGTGGG GGGACTGCTCAGGAGTGATGGTGCCCTGGAGTTTGCCCTGGCCACCTCCTCCG GGTGCCTGGCTGCTCCAGGCCTCTAGGCTGGGCTGATGGGTTTCTCCAGGACACAAGTATC ATTAAAGCCACCCTCTCCTCAGCTTGTCAGGCCGCACATGTGGGACACAGGCTGTGCTCACAA CATCTCAGCAGCCCTCCATCAGGAGGAGCCAGTGGAACCTTCGGAAAAGCTCCCAG CATCTCAGCAGCCCTCAAAAGTCCCTGGGGCCAAGCTCTGGGAAAGCTCCCAG CATCTCAGCAGCCCTCCAAAAAGTCCCTGGGGCCAAGCTCTGGTTCTCCTGACTGGAGGTCA

### 171843

TAAAAAAGTGTAACAAAGGTTTATTTAGACTTTCTTCATGCCCCCAGATCCAGGATGTCTA
TGTAAACCGTTATCTTACAAAGAAAGCACAATATTTGGTATAAACTAAGTCAGTGACTTGC
GGGGATCCTGCAGTTTGGACTTGCCGGGTTTAAGGTAAAACTACCTGACGATATTTGGC
GGGATCCTGCAGTTTGGACTGCTGCCGGGTTTCCAGGGTTCCGGGTCTGTTCTTGGC
GAAGGTATCGACCSTAGGGGGCTCTAGGGGCCCCGCTGGAGCCCTTACGTGAAGCT
GCGGGGACAGCCTTACGTGGGGACCTTCATCCGGAACCTTAACAAGGG
TCGGGGAAACCTAACAAGGG

CAAGCGTTCCTTTATGGATGTAAATTCAAACAGTCATGCTGAGCCATCCCGGGCTGACAGT CACGTTWAAGACACTAGGTCGGGCGCCACAGTGCCACCCAAGGAGAAGAATTTGGA ATTTTTCCATGAAGATGTACGGAAATCTGATGTTGAATATGAAAATGGCCCCCAAATGGAA TCCAAAAGGTTACCACAGGGGCTGTAAGACCTAGTGACCCTCCTAAGTGGGAAAGAGGA ATGGAGAATATTTCTGATGCATCAAGAACATCAGAATATAAAACTGAGATCATAATG AAGGAAAATTCCATATCCAAGAATATCCCAGATATCCCAGG

## 17185.1

TAGGAATAACAAATGTTTATTCAGAAATGGATAAGTAATACATAATCACCCTTCATCTCTT
AATGCCCCTTCCTCTCTCTCCACAGGAGACACAGATGGGTAACATAGAGGCATGGGAA
GTGGAGGAGGACACAGGACTAGCCCACCACCTTCTCTCCCGGTCTCCCCAAGATGACTGCT
TATAGAGTGGAGGAGGCAAACAGGTCCCCTCAATGTACCAGATGGTCACCTATAGCACCA
GCTCCAGATGGCCACGTGGTTGCAGCTGGACTCAATGAAACTCTGTGACAACCAGAAGAT
ACCTGCTTTGGGATGAGAGGGAGGATAAAGCCATGCAGGGAGGATATTTACCATCCCTAC
CCTAAGCACAGTGCAAGCAGTGAGCCCCCGGCTCCCAGTACCTGAAAAAACCAAGGCCTAC
TGNCTTTTGGATGCTCTCTTGGGCCACG

#### 17133.2

## 17190.1

# 17191\_2&89.2

AGCCAGATGGCTGAGAGCTGCAAGAAGAAGTCAGGATCATGATGGCTCAGTTTCCCACAG CGATGAATGGAGGGCCAAATATGTGGGCTATTACATCTGAAGAACGTACTAAGCATGATA AACAGTTTGATAACCTCAAACCTTCAGGAGGTTACATAACAGGTGATCAAGCCCGTACTTT TTTCCTACAGTCAGGTCTGCCGGCCCCGGTTTTAGCTGAAATATGGGCCTTATCAGATCTG AACAAGGATGGGAAGATGGACCAGCAAGAGTTCTCTATAGCTATGAAACTCATCAAGTTA AAGTTGCAGGGCCAACAGCTGCCTGTAGTCCTCCCTATCATGAAACAACCCCCTATGT TCTCTCCACTAATCTCTGCTCGTTTTGGGATGGGAAGCATGCCCAATCTGTCCATTCATCAG CCATTGCCTCCAGTTGCACCTATAGCAACACCCTTGTCTTCTGCTACTTCAGGGACCAGTAT TCCTCCCCTAATGATGCCTGCTCCCCTAGTGCCTTCTGTTAGTACATCCTCATTACCAAATG GAACTGCCAGTCTCATTCAGCCTTTATCCATTCCTTATTCTTCAACATTGCCTCATGCA TCATCTTACAGCCTGATGATGGGAGGATTTGGTGGTGCTAGTATCCAGAAGGCCCAGTCTC TGATTGATTTAGGATCTAGTAGCTCAACTTCCTCAACTGCTTCCCTCTCAGGGAACTCACCT AAGACAGGGACCTCAGAGTGGGCAGTTCCTCAGCCTTCAAGATTAAAGTATCGGCAAAAA TTTAATAGTCTAGACAAAGGCATGAGCGGATACCTCTCAGGTTTTCAAGCTAGAAATGCCC TTCTTCAGTCAAATCTCTCTCAAACTCAGCTAGCTACTATTTGGACTCTGGCTGACATCGAT GGTGACGGACAGTTGAAAGCTGAACAATTTATTCTGGCGATGCACCTCACTGACATGGCC AAAGCTGGACAGCCACTACCACTGACGTTGCCTCCCGAGCTTGTCCCTCCATCTTTCAGAG GGGGAAAGCAAGTTGATTCTGTTAATGGAAČTCTGCCTTCATATCAGAAAACACAAGAAG AAGAGCCTCAGAAGAAACTGCCAGTTACTTTTGAGGACAAACGGAAAGCCAACTATGAAC GAGGAAACATGGAGCTGGAGAAGCGACGCCAAGTGTTGATGGAGCAGCAGCAGAGGGAG AACAGGAGCTTGAGAGACAACGCCGTT.AGAATGGGAAAGACTCCGTCGGCAGGAGCTGC CTCCACCTGGAACTGGAAGCAGTGAATGGAAAACATCAGCAGATCTCAGGCAGACTACAA GATGTCCA.A.ATCAGA.A.AGCA.A.ACACA.A.A.AGACTGAGCTAGA.AGTTTTGGATAAACAGTGT GACCTGGAAATTATGGAAATCAAACAACTTCAACAAGAGCTTAAGGAATATCAAAATAAG CTTATCTATCTGGTCCCTUAGAAGCAGCTATTAAACGAAAGAATTAAAAACATGCAGCTCA GTAACACACCTGATTCAGGGATCAGTTTACTTCATAAAAAGTCATCAGAAAAGGAAGAAT TATGCCAAAGACTTAAAGAACAA TTAGATGCTCTTGAAAAAGAAACTGCATCTAAGCTCT CAGAAATGGATTCATTTAACAATCAGCTGAAGGAACTCAGAGAAAGCTATAATACACAGC AGTTAGCCCTTGAACAACTTCATAAAATCAAACGTGACAAATTGAAGGAAATCGAAAGAA AAAGATTAGAGCAA.4.4.4.4.4.4.4.4.4.4.4.

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GAAGAGAGCACCCAGTGTTGGGCTGAAAACATCTGAAAGTAGGGAGAAGAACCTAAAAT
AATCAGTATCTCAGAGGGCTCTAAGGTGCCAAGAAGTCTCACTGGACATTTAAGTGCCAA
CAAAGGCATACTTTCGGAATCGCCAAGTCAAAACTTTCTAACTTCTGTCTCTCAGAGAC
AAGTGAGACTCAAGAGTCTACTGCTTTAGTGGCAACTACAGAAAACTGGTGTTACCCAGA
AAACAGGAGCAATTAGAAATGGTTCCAATATTTCAAAGCTCCGCAAACAGGATGTGCTT
ICCTTTGCCCATTTAGGGTTTCTCTTTTCCTTTTCTTTTATTAACCACTA

ATATCTAGAAGTCTGGAGTGAGCAAACAAGAGCAAGAAACAAAAGAAGCCAAAAGCAG AAGGCTCCAATATGAACAAGATAAATCTATCTTCAAAGACATATTAGAAGTTGGGAAAAT AATTCATGTGAACTAGACAAGTGTGTTAAGAGTGATAAGTAAAATGCACGTGGAGACAAG TGCATCCCCAGATCTCAGGGACCTCCCCCTGCCTGTCACCTGGGGAGTGAGAGGACAGGAT AGTGCATGTTCTTTGTCTCTGAATTTTTAGTTATATGTGCTGTAATGTTGCTCTGAGGAAGC CCCTGGAAAGTCTATCCCAACATATCCACATCTTATATTCCACAAATTAAGCTGTAGTATG TACCCTAAGACGCTGCTAATTGACTGCCACTTCGCAACTCAGGGGCGGCTGCATTTTAGTA ATGGGTCAAATGATTCACTTTTTATGATGCTTCCAAAGGTGCCTTGGCTTCTCTTCCCAACT GACAAATGCCAAAGTTGAGAAAAATGATCATAATTTTAGCATAAACAGAGCAGTCGGCGA CAGATGATGTTCATCCGTGAATGGTCCAGGGAAGGACCTTTCACCTTGACTATATGGCATT ATGTCATCACAAGCTCTGAGGCTTCTCCTTTCCATCCTGCGTGGACAGCTAAGACCTCAGT TTTCAATAGCATCTAGAGCAGTGGGACTCAGCTGGGGTGATTTCGCCCCCCATCTCCGGGG GAATGTCTGAAGACAATTTTGTTACCTCAATGAGGGAGTGGAGGAGGATACAGTGCTACT ACCAACTAGTGGATAAAGGCCAGGGATGCTGCTCAACCTCCTACCATGTACAGGACGTCTC CCCATTACAACTACCCAATCCGAAGTGTCAACTGTGTCAGGACTAAGAAACCCTGGTTTTG ATTGGCAAATAAGCATTCTGTCTCTTTGGCTGCTGCCTCAGCACAGAGAGCCAGAACTCTA TCGGGCACCAGGATAACATCTCTCAGTGAACAGAGTTGACAAGGCCTATGGGAAATGCCT CCAAGTTCTGTAAGAGAAATGCCTGAGTTCTAGCTCAGGTTTTCTTACTCTGAATTTAGATC CACACAGACTTTTGAAAGCAAGGACAATGACTGCTTGAATTGAGGCCTTGAGGAATGAAG CTTTGAAGGAAAAGAATACTTTGTTTCCAGCCCCCTTCCCACACTCTTCATGTGTTAACCAC TGCCTTCCTGGACCTTGGAGCCACGGTGACTGTATTACATGTTGTTATAGAAAACTGATTTT AGAGTTCTGATCGTTCAAGAGAATGATTAAATATACATTTCCTA

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FIG. 3

TAGCGYGGTCGCGGGCCGAGGYCTGCTTYTCTGTCCAGCCCAGGGCCTGTGGGGTCAGGGC GGTGGGTGCAGATGGCATCCACTCCGGTGGCTTCCCCCATCTTTCTCTGGCCTGAGCAAGGT CAGCCTGCAGCCAGAGTACAGAGGGCCAACACTGGTGTTCTTGAACAAGGGCCTTAGCAG GCCCTGAAGGRCCCTCTCTGTAGTGTTGAACTTCCTGGAGCCAGGCCACATGTTCTCCTCAT ACCGCAGGYTAGYGATGGTGAAGTTGAGGGTGAAATAGTATTMANGRAGATGGCTGGCA

AGCGTGGTCGCGGCCGAGGTGTCCTTCAGGGTCTGCTTATGCCCTTGTTCAAGAACACCAG TGTCAGCTCTCTGTACTCTGGTTGCAGACTGACCTTGCTCAGGCCTGAGAAGGATGGGGCA GCCACCAGAGTGGA TGCTGTCTGCACCCATCGTCCTGACCCCAAAAGCCCTGGACTGGACA GAGAGCGGCTGTACTGGAAGCTGAGCCAGCTGACCCACGGCATCACTGAGCTGGGCCCCT ACACCCTGGACAGGGACAGTCTCTATGTCAATGGTTTCACCCATCGGAGCTCTGTACCCAC CACCAGCACCGGGGTGGTCAGCGAGGAGCCATTCAACCTGCCCGGGCCGCCCCGA WO 00/36107 PCT/US99/30270

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B AGCGTGGTCGCGGCCGAGGTCCAGTCGCAGCATGCTCTTTCTCCTGCCCACTGGCACAGTG
AGGAAGATCTCTGCTGTCAGTGAGAAGGCTGTCATCCACTGAGATGGCAGTCAAAAGTGC
ATTTAATACACCTAACGTATCGAACATCATAGCTTGGCCCAGGTTATCTCATATGTGCTCA
GAACACTTACAATAGCCTGCAGACCTGCCCGGGCGGCCGCTCGA

TGTGGTGTTGAACTTCCTGGAGNCAGGGTGACCCATGTCCTCCCCATACTGCAGGTTGGTG
ATGGTGAAGTTGAGGGTGAATGGTACCAGGAGAGGGCCAGCAGCAGCATAATTGTSGRGCKG
SMGMSSGAGGMWGGWGTYYCWGAGGTTCYRARRTCCACTGTGGAGGTCCCAGGAGTGCT
GGTGGTGGGGACAGAGSTCYGATGGGTGAAACCATTGACATAGAGACTGTTCCTGTCCAG
GGTGTAGGGGCCCAGCTCTTYRATGYCATTGGYCAGTTKGCTYAGCTCCCAGTACAGCCRC
TCTCKGYYGMGWCCAGSGCTTTTGGGGTCAAGATGATGGATGCAGTCCACTCCA
GTGGCTGCTCCATCCTTCTCGGACCTGAGAGAGGGTCAGTCTGCAGCCAGAGTACAGAGGG
CCAACACTGGTGTTCTTTGAATA

TCGAGCGGCCGCCCGGGCAGGTCAGGAAGCACATTGGTCTTAGAGCCACTGCCTCCTGGA TTCCACCTGTGCTGCGGACATCTCCAGGGAGTGCAGAAGGGGAAGCAGGTCAAACTGCTCA GATCAGTCAGACTGGCTGTTCTCAGTTCTCACCTGAGCAAGGTCAGTCTGCAGCCAGAGTA CAGAGGGCCAACACTGGTGTTCTTGAACAAGGGCTTGAGCAGACCCTGCAGAACCCTCTTC CGTGGTGTTGAACTTCCTGGAAACCAGGGTGTTGCATGTTTTTCCTCATAATGCAAGGTTG

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#### 11721-1

#### 11721-2

### 117241

TITGITCCTTACATTITICTA.AAGAGTTACTTAAATCAGTCAACTGGTCTTTGAGACTCTTA
AGTTCTGATTCCAACTTAGCTAATTCATTCTGAGAACTGTGGTATAGGTGGCGTGTCTCTTC
TAGCTGGGACAAAAAGTTCTTTGTTTTCCCCCCTGTAGAGTATCACAGACCTTCTGCTGAAGC
TGGACCTCTGTCTGGGCCTTGGACTCCCAAATCTGCTTGTCATGTTCAAGCCTGGAAATGTT
AATCTTAATTCTTCCATATTGGATGGACATCTGTTGATCCTTTAGAACACTGCAAT
TATCTTCTTTGAGTCTAATTTCTTCTTCTTTGATCCATCACTAAACTTCCTCTCCCCAT
ATTCTTAGCTTCATCTATCACCCTGTCACGATCATCCTTGAGACACTTCCTCTCCC
AAGGCTGCAAGCTGGGTCACAGTACTGTCCAAGTTTCCTGAAGTTGCTGAACTTCCTTTAGTA
CTTTCTTTGTTCAAAGTAACCTGAATCTCTCCCAAGTTTTCCTGAAGTTGCTGAACTTCCTTGT
CAAAGCATCCAG

# 117242

# 11725-32-1.2

#### 11726-1&2

### 11727-1&2

#### 11728.1.40.19.19

# 11728.2.40.19.19

## 11730-1

# 11730-3

# 11732.1contig

### 11732.2contig

#### 11735-1-2

AGATCAACCTCTGCTGGTCAGGAGGAATGCCTTCCTTGTCTTGGATCTTTGCTTTGACGTTC
TCGATAGTRWCA2CTKKRYTSRAMSKMAAGKGYRATGRWMTTKSYWGWRASYKTMWWM
RSGRARAYTT3G2CAYCCCMCCTCW2AG2CGSAGKACCARGTGCA2A3GTGGACTCTTTCTG
GATGTTGTAGTCAGACAGGGTGCGTCCATCTTCCAGCTGTTTCCCAGCAAAGATCAACCTC
TGCTGATCAGGAGGGATGCCTTCCTTATCTTGGATCTTTGCCTTGACATTCTCGATGGTGTC
ACTGGGCTCCACCTCGAGGGTGATGGTCTTACCAGTCAGGGTCTTCACGAAGATYTGCATC
CCACCTCTGAGACGGAGCACCAGGTGCAGGGTRGACTCTTTCTGGATGTTGTAGTCAGACA
GGGTGCGYCCATCTTCCAGCTGCTTTCCS2GCAAAGATCAACCTCTGGTCAGGAGGRAT
GCCTTCCTTGTCYTGGATCTTTGCYTTGACRTTTCTCRATGGTGTCACTCGGCTCCACTTCGA
GAGTGATGGTCTTACCAGTCAGGGTCTTCACGAAGATCTCCCACCTCTAA

# 11740.2.contig

# 11763.2&64.2 contig

CGCCTCCACCATGTCCATCAGGGTGACCCAGAAGTCCTACAAGGTGTCCACCTCTGGCCCC CGGGCCTTCAGCAGCCGCTCCTACACGAGTGGGCCCGGTTCCCGCATCAGCTCCTCGAGCT TCTCCCGAGTGGGCAGCAGCAACTTTCGCGGTGGCCTGGGCGGCGGCTATGGTGGGGCCA GCGGCATGGGAGGCATCACCGCAGTTACGGTCAACCAGAGCCTGCTGAGCCCCCTTGTCCT GGAGGTGGACCCC.AACATCC.AGGCCGTGCGCACCC.AGGAGAAGGAGCAGATCAAGACCCT CAACAACAAGTTTGCCTCCTTCATAGACAAGGTACGGTTCCTGGAGCAGCAGAACAAGAT GCTGGAGACCAAGTGGAGCCTCCTGCAGCAGCAGCAGCAGCGCTCGAAGCAACATGGACA ACATGTTCGAGAGCTACATCAACARCCTTAGGCGGCAGCTGGAGACTCTGGGCCAGGAGA AGCTGAAGCTGGAGGCGGAGCTTGGC.4ACATGCAGGGGCTGGTGGAGGACTTCÁAGAAC AAGTATGAGGATGAGATCAATAAGCGTACAGAGATGGAGAACGAATTTGTCCTCATCAAG AAGGATGTGGATGAAGCTTACATGAACAAGGTAGAGCTGGAGTCTCGCCTGGAAGGGCTG ACCGACGAGATCAACTTCCTCAGGCAGCTGTATGAAGAGGAGATCCGGGAGCTGCAGTCC CAGATCTCGGACACATCTGTGGTCCTGTCCATGGACAACAGCCGCTCCCTGGACATGGACA GCATCATTGCTGAGGTCAAGGCACAGTACGAGGATATTGCCAACCGCAGCCGGGCTGAGG CTGAGAGCATGTACCAGGTCAAGTATGAGGĀGCTGCAGAGCCTGGCTGGGAAGCACGGGG ATGACCTGCGGCGCACAAAGACTGAGATCTCTGAGATGAACCCGGAACATCAGCCCGGCT XCAGGCTGAGATTGAGGGCCTCAAAGGCCAGAXGGCTTXCCTGGAXGXCCGCCAT

# 11767.2.contig

CCCGGAGCCAGCCAACGAGCGGAAAATGGCAGACAATTTTTCGCTCCATGATGCGTTATCT
GGGTCTGGAAACCCAAACCCTCAAGGATGGCTGGCGCATGGGGGGAACCAGCCTGCTGGG
GCAGGGGGCTACCCAGGGGCTTCCTATCCTGGGGCCTACCCCGGGCAGCACCCCCAGGG
GCTTATCCTGGACAGGCACCTCCAGGCGCCTACCCTGGAGCACCTGGAGCTTATCCCGGAG
CACCTGCACCTGGAGTCTACCCAGGGGCACCCACCGGCCCTGGGGCCTACCCATCTTCTGG
ACAGCCAAGTGCCACCGGAGCCTACCCTGCGCCCTATGGCGCCCTGCTGGGCCA
CTGATTGTGCCTTATAACCTGCCTTTGCCTGGGGGAGTGGTGCTCGCATGCTGATAACAA
TTCTGGGCACGGTGAAGCCCAATGCAAAACAGAATTGCTTTAGATTTCCAAAGAGGGAATG
ATGTTGCCTTCCACTTTAACCCCACGCTTCAATGAGAACAACAGAGGGAATG
TACAAAGCTGGATAA

## 11768-13:

GGGAATGCAACAACTITATTGAAAGGAAAGTGCAATGAAATTTGTTGAAACCTTAAAAGG
GGAAACTTAGACACCCCCCCCTCRAgCGMAGKACCARGTGCARAgGTGGACTCTTTCTGGAT
GTTGTAGTCAGACAGGGTRCGWCCATCTTCCAGCTGTTTYCCRGCAAAGATCAACCTCTGC
TGATCAGGAGGRATGCCTTCCTTATCTTGGATCTTTGCCTTTGACATTCTCGATGTGTCACT
GGGCTCCACCTCGAGGGTGATGGTCTTACCAGTCACGGGTCTTCACGAAGATYTGCATCCCA
CCTCTGAGACGGAGCACCAGGTGCAGGGTRGACTCTTTCTGGATGTTGTAGTCAGACAGG
GTGCGYCCATCTTCCAGCTGeTTTCCS2GCAAAAGATCAACCTCTGCTGGTCAGGAGGRATGC
CTTCCTTGTCYTGGATCTTTGCYTTGACRTTCTCAATGGTGTCACTCGGCTCCACTTCGAGA
GTGATGGTCTTACCAGTCAGGGTCTTCACGAAGATCTCCCACCTCTAAGACGGAGCA
CCAGGTGCAGGGTGGACTCTTTCTGGGATGGTTAGTCAGACAGGGTGCACCCCACTTCCAAGGCTCCACTTCCCA
CCAGGTGCAGGGTGGACTCTTTCTGGGATGGTTGTAGTCAGACAGGGTGCACCCCACTTCCCACGCACCTCTTAAGACGGAGCA

# 11768-1&2-11735-1&2

AGGTTGATCTTTGCTGGGAAACAGCTGGAAGATGGACGCACCCTGTCTGACTACAA¢CATC
CAGAAAGAGTCCACCCTGCACCTGGTGCTCCGTCTTAGAGGTGGGATGCAGATCTTCGTGA
AGACCCTGACTGGTAAGACCATCACTCTCGAAGTGGAGCCGAGTGACACCATTGAGAAYG
TCAARGCAAAGATCCARGACAAGGAAAGGCATYCCTCCTGACCAGCAGAGGTTGATCTTTG
CISGGAAAgCAGCTGGAAGATGGRCGCACCCTGTCTGACTACAACATCCAGAAAGAGTCYA
CCCTGCACCTGGTGCTCCGTCTCAGAGGTGGGATGCARATCTTCGTGAAGACCCTGACTGG
TAAGACCATCACCCTCGAGGTGGAGCCCAGTGACACCATCGAGAATGTCAAGGCAAAGAT
CCAAGATAAGGAAGGCATCCCTCCTGATCAGCAGAGGTTGATCTTTGCTGGGAAACAGCT
GGAAGATGGACGCACCCTGTCTGACTACAACATCCAGAAAGAGTCCACCTYTGCACYTGGT
MCTBCGTCTY3GAGGKGGGRTGc3223TCTWMGTKW3g3C3CtC3CTKKYAAGRYY3TCAMCMWt
gAKKTCgAKYSCASTKWC3CTWTCRAKAAMGTYRWWGCAW3g3TCCMAGACAAGGACA

# 11769.1.contig

# 11-69.2.contig

# 11 70.1.contig

# 11770.2.contig

GCAAGGAACTGGTCTGCTCACACTTGCTGGCTTGCGCATCAGGACTGGCTTTATCTCCTGA GGCCCCCACAGCCGGATCCCCTCAGCCTTCCAGGTCCTCAACTCCCGTGGACGCTGAACAA TGGCCTCCATGGGGCTACAGGTAATGGGCATCGCGCTGGCCGTCCTGGGCTGGCCGT CATGCTGTGCTGCGCGCTGCCCATGTGGCGCGTGACGGCCTTCATCGGCAGCAACATTGTC ACCTCGCAGACCATCTGGGAGGGCCTATGGATGAACTGCGTGGTGCAGAGCACCGGCCAG ATGCAGTGCAAGGTGTACGACTCGCTGCTGGCACTGCCGCAGGACCTGCAGGCGGCCCGC

# 11773.1.contig

TGCAAAAGGGACACAGGGGTTCAAAAATTTCTCTTCCCCCTCCCCAAACCTGTAC CCCAGCTCCCCGACCACAACCCCCTTCCTCCCCCCGGGGAAAGCAAGAAGGAGCAGGTGTG GCATCTGCAGCTGGGAAGAGAGGCCGGGGGAGGTGCCGAGCTCGGTGCTGTTTTC GCGGTCTACTGCATCCGCTGGGTGTGCACCCCGCGAGCCTCCTGCTGCTCATTGTAGAAGA GATGACACTCGGGGTCCCCCGGATGGTGGGGGGCTCCCTGGATCAGCTTCCCGGTGTTGGG GTTCACACACCAGCACTCCCCACGCTGCCCGTTCAGAGACATCTTGCACTGTTTGAGGTTG

# 11773.1.contig

GGGTTGGAGGGACTGGTTCTTTATTTCAAAAAAGACACTTGTCAATATTCAGTATCAAAAACA GTTGCACTATTGATTTCTCTCTCCCAATCGGCCCCAAAGAGACCACATAAAAGGAGAGT ACATTTTAAGCCAATAAGCTGCAGGATGTACACCTAACAGACCTCCTAGAAACCTTACCAG CTGCAGAGGCTGTCACAGCCAGATGGGGTGGCCAGGGTGCCCACAAAGCCAAAGCAAAGTT TCAAAATAATAAAAATTTAAAAAAGTTTTGTACATAAGCTATTCAAGATTTCTCCAGCACT GACTGATACAAAGCACAATTGAGATGGCACTTCTAGAGACAGCAGCAGCTTCAAACCCAGAAA AGGGTGATGAGATGAGTTTCACATGGCTAAATCAGTGGCAAAAACACAGTCTTCTTT CTTTCTTTCAAGGAGGCAGGAAAGCAATTAAGTGGTCACCTCAACATAAGGGGGACATGA TCCATTCTGTAAGCAGTTGTGAAGGGG

# 11778-2830-2

CAGGAACCGGAGCGCGAGCAGTAGCTGGGTGGGCACCATGGCTGGGATCACCACCATCGA CTGAGCGCCTCCAGCGAGAAGTTGAGGGAGAAAGGCGGGCCCGGGAACAGGCTGAGGCT GAGGTGGCCTCCTTGAACCGTAGGATCCAGCTGGTTGAAGAAGAGCTGGACCGTGCTCAG GAGCGCCTGGCCACTGCCCTGCALAAGCTGGAAGAAGCTGAAALAAGCTGCTGATGAGAGT GAGAGAGGTATGAAGGTTA.TGAAAACCGGGCCTTAAAAGATGAAGAAAAAGATGGAACT CCAGGAAATCCAACTCAAAGAAGCTAAGCACATTGCAGAAGAGGCCAGATAGGAAGTATG AAGAGGTGGCTCGTAAGTTGGTGATCATTGAAGGAGGACTTGCAACGCACAGAGGAACGAG CTGAGCTGGCAGAGTCCCGTTGCCGAGAGATGGATGAGCAGATTAGACTGATGGACCAGA

# 11782.1.contig

ATCTACGTCATCAATCAGGCTGGAGACACCATGTTCAATCGAGCTAAGCTGCTCAATATTG
GCTTTCAAGAGGCCTTGAAGGACTATGATTACAACTGCTTTGTGTTCAGTGATGTGGACCT
CATTCCGATGGACGACCGTAATGCCTACAGGTGTTTTTCGCAGCCACGGCACATTTCTGTT
GCAATGGACAAGTTCGGGTTTAGCCTGCCATATGTTCAGTATTTTGGAGGTGTCTCTGCTCT
CAGTAAACAACAGTTTCTTGCCATCAATGGATTCCCTAATAATTATTGGGGTTGGGGAGGA
GAAGATGACGACATTTTTAACAGATTAGTTCATAAAGGCATGTCTATATCACGTCCAAATG
CTGTAGTAGGGAGGTGTCGAATGATCCGGCATTCAAGAGAAAAAATGAGCCCAATC
CTCAGAGGTTTGACCGGATCGCACATACAAAGGAAACGATGCGCTTCGATGGTTTGAACT
CACTTACCTACAAGGTGTTGGATGTCAGAGAGATACCCGTTATATACCCAAATCAC

# 11782.2.contig

# 11783-1 & 2

## 11736.1.contig

# 11786.2.contig

## 13691.1&2

# 13692.1&2

TCCGAATTCCAAGCGAATTATGGACAAACGATTCCTTTTAGAGGATTACTTTTTCAATTTC
GGTTTTAGTAATCTAGGCTTTGCCTGTAAAGAATACAACGATGGATTTAAATACTGTTTG
TGGAATGTGTTTAAAGGATTGATTCTAGAACCTTTGTATATTTGATAGTATTCTAACTTTC
ATTTCTTTACTGTTTGCAGTTAATGTTCATGTTCATGCTATGCAATCGTTTATATGCACGTTTC
TTAATTTTTTTAGATTTTCCTGGATGTATAGTTTAAAACAACAAAAAGTCTATTTAAAACTG
TAGCAGTAGTTTACAGTTCTAGCAAAGAGGAAAGTTGTGGGGGTTAAACTTTGTATTTTCTT
TCTTTATAGAGGCTTCTAAAAAAGGTATTTTATATATGTTCTTTTTAACAAATATTTGTGTACAAC
CTTTAAAAACATCAATGTTTGGATCAAAACAACAAGACCCCAGCTTATTTTCTC

## 13693.2

TGTGGTGGCGCGGGCTGAGGTGGAGGCCCAGGACTCTGACCCTGCCCTGCCTTCAGCAA
GGCCCCCGGCAGCGCCGCCACTACGAACTGCCGTGGGTTGAAAAATATAGGCCAGTAAA
GCTGAATGAAATTGTCGGGGAATGAAGACACCGTGAGCAGGCTAGAGGTCTTTGCAAGGGA
AGGAAATGTGCCCAACATCATCATTGCGGGCCCTCCAGGAACCGGCAAGACCACAAGCAT
TCTGTGCTTGGCCCGGGCCCTGCTGGGCCCCAGCACTCAAAGATGCCATGTTGGAACTCAAT
GCTTCAAATGACAGGGGCATTGACGTTGTGAGGAATAAAATTAAAATGTTTGCTCAACAA
AAAGTCACTCTTCCCAAAGGCCGACATAAGATCATCATTCTGGATGAAGCAGCACCATG
ACCGACGGACCCCAGCAAGCCTTGAGGAGAACCATGGAAATCTACTCTAAAACCACTCGT
TCGCCCTTGCTTGTAATGCTTCGGATAACATCATCATCACCACCCCTCGT

### 13696.1-13744.1

### 13700.1

#### 13700.2

## 13701.1

AAAAAGCAGCARGTTCAACACAAATAGAAATCTCAAATGTAGGATAGAACAAAACCAA GTGTGTGAGGGGGGAAGCAACAGCAAAAGGAAGAAATGAGATGTTGCAAAAAAGATGGA GGAGGGTTCCCCTCTCGGGGACTGACTCAAACACTGATGTGGCAGTATACACCATTC CAGAGTCAGGGGTGTTCATTCTTTTTTGGGAGTAAGAAAAGGTGGGGGATTAAGAAGACGT TTCTGGAGGCTTAGGGACCAAGGCTGGTCTCTTTTCCCCCCCTCCCAACCCCCTTGATCCCTTT CTCTGATCAGGGGAAAGGAGCTCGAATGAGGGAGGTAGAGTTGGAAAGGGAAAGGATTC CACTTGACAGAATGGGACAGACTCCTTCCCA

### 13702.2

AGCTGGCGCTAGGGCTCGGTTGTGAAATACAGCGTRGTCAGCCCTTGCGCTCAGTGTAGAA ACCCACGCCTGTAAGGTCGGTCTTCGTCCATCTGCTTTTTTCTGAAATACACTAAGAGCAG CCACAAAACTGTAACCTCAAGGAAACCATAAAGCTTGGAGTGCCTTAATTTTTAACCAGTT TCCAATAAAACGGTTTACTACCT

# 13704.2-13740.2

GGAGATGAAGATGAGGAAGCTGAGTCAGCTACGGGCARGCGGGCAGCTGAAGATGATGA GGATGACGATGTCGATACCAAGAAGCAGAAGACCGACGAGGATGACTAGACAGCAAAAA AGGAAAAGTTAAA

### 13706.1

GATGAAAATTAAATACTTAAATTAATCAAAAGGCACTACGATACCACCTAAAACCTACTG CCTCAGTGGCAGTAKGCTAAKGAACATCAAGCTACAGSACATYATCTAATATGAATGTTA GCAATTACATAKCARGAAGCATGTTTGCTTTCCAGAAGACTATGGNACAATGGTCATTWG GGCCCAAGAGGATATTTGGCCNGGAAAGGATCAAGATAGATNAANGTAAAG

### 13706.2

## 13707.3

## 13710.2

AGGTTGGAGAAGGTCATGCAGGTGCAGATTGTCCAGGSKCAGCCACAGGGTCAAGCCCAA
CAGGCCCAGAGTGGCACTGGACAGACCATGCAGGTGATGCAGCAGATCATCACTAACACA
GGAGAGATCCAGCAGATCCCGGTTGCAGCTGAATGCCGGCCAGCTGCAGTATATCCGCTTA
GCCCAGCCTGTATCAGGCACTCAAGTTGTGCAGGGACAGATCCAGACACTTGCCACCAAT
GCTCAACAGATTACACAGACAGAGGTCCAGCAAGGACAGCAGCAGTTCAAGCCAGTTCAC
AAGATGGACAGCAGCTCTACCAGATCCAGCAAGTCACCATGCCTGCGGGCCANGACCTCG
CCAGCCCATGTTCATCCAGTCAAGCCAACCAGCCCTTCNACGGGCAGGCCCCCCAGGTGAC
CGGCGACTGAAGGGCCTGACCTGGCAAGGCCAANGACACCCAACACATTTTTTGCCATAC
AGCCCCCAGGCAATGGGCAATGGCCAACGACCACCAATTTTTTTGCCATAC

## 13710-1

## 13711.1

### 13711.2

TGAGACGGACCACTGGCCTGGTCCCCCCTCATKTGCTGTCGTAGGACCTGACATGAAACGC
AGATCTAGTGGCAGAGAGGAAGATGATGAGGAACTTCTGAGACGTCGGCAGCTTCAAGAA
GAGCAATTAATGAAGCTTAACTCAGGCCTGGGACAGTTGATCTTGAAAGAAGAGATGGAG
AAAGAGAGCCGGGAAAGGTCATCTCTGTTAGCCAGTCGCTACGATTCTCCCATCAACTCAG
CTTCACATATTCCATCATCTAAAACTGCATCTCTCCCTGGCTATGGAAGAAATGGGCTTCA
CCGGCCTGTTTCTACCGACTTCGCTCAGTATAACAGCTATGGGGATGTCAGCGGGGGGGTG
CGAGATTACCAGACACTTCCAGATGGCCACATGCCTGCAATGAGAATGGACCGAGGAGTG
ICTATGCCCAACATGTTGGAACCAAAGATATTTCCATATGAAAATGCTCATGGTGACCAACA
GAGGGCCGAAACCAAATCTCAGAGAGGTGGACAGAA

# 13713.1&2

TCACTITATTITCTTGTATAAAAACCCTATGTTGTAGCCACAGCTGGAGCCTGAGTCCGCT GCACGGAGACTCTGGTGTGGGTCTTGACGAGGTGGTCAGTGAACTCCTGATAGGGAGACT TGGTGAATACAGTCTCCTTCCAGAGGTCGGGGGTCAGGTAGCTGTAGGTCTTAGAAATGGC ATCAAAGGTGGCCTTGGCGAAGTTGCCCAGGGTGGCAGTGCAGCCCCGGGCTGAGGTGTA GCAGTCATCGATACCAGCCATCATGAG

## 13715.4

# 13717.132

### 13719.1&2

### 13721.1

#### 13721.2

## 13723.1

WO 00/36107 49 / 92 PCT/US99/30270

## 13723.2

GAIGIGTTGGACCCTCTGTGTC.AAAAAAAACCTC.ACAAAGAATCCCCTGCTCATTACAGAA
GAAGATGCA.FITAAAATA.TGGGTTA.ITTTC.AACTTTTTATCTGAGGACAAGTATCCATTAA
TTATTGTGTCAGAAGAGATTGAATACCTGCTTAAGAAGCTTACAGAAGCTATGGGAGGAG
GTTGGC.AGCAAGAACAA.TTTGAACA.TT.ATAAAATCCAACTTTGATGACAGTAAAAATGGCC
TTTCTGCATGGGAACTTA.TTGAGCTTA.TTGGAAATGGACAGTTTAGCAAAGGCATGGACCG
GCAGACTGTGTCTATGGCAATTAATGAAGTCTTTAATGAACTTATATTAGATGTGTTAAAG
CAGGGTTACATGATGAAAAAAGGGCCACAGACGGAAAAAACTGGACTGAAAGATGGTTTGTA
CTAAAACCCAACATAATTTCTTACTATGTGAGTGAGGATCTGAAGGATAAGAAGGAGAC
ATTCTCTTGGATGAAAAATTGCTGTGTAGAAGTCCTTGCCTGACAAAAAGATGGAAAAAT
GCCTTTT

### 13725.1

## 13725.2

TGGGTGGGCACCATGGCTGGGATCACCACCATCGAGGCGGTGAAGCCGCAAGATCCAGGTT CTGCAGCAGCAGGCAGATGATGCAGAGGAGCAGCGAGCTGAGCGCCTCCAGCGAGAAGTTGA GGGAGAAAGGCGGGCCCGGGAACAGGCTGAGGCTGAGGTGGCCTCCTTGAACCGTAGGA TCCAGCTGGTTGAAGAAGAGCTGGACCGTGCTCAGGAGCGCCTGGCCACTGCCCTGCAAA AGCTGGAAGAAGCTGAAAAAGCTGCTGATGAGAGTGAGAGGTATGAAGGTTATTGAA AACCGGGCCTTAAAAGATGAAGAAAAGATGGAACTCCAGGAAATCCAACTCAAAGAAGC TAAGCACATTGCAGAAGAAGAAGAAGAAGTATGAAGAGGTGGCTCGTAAGTTGGTGAT CATTGAAGGAGACTTGGAACCGCACAGAAGGAACGAGCTTGACCTTGGCAAAAGTCCCGT

# 13726.1&2

## 13727.1

### 13727.2

ACCTAGACAGAAGGTGGGTGAGGGAGGACTGGTAGGAGGCTGAGGCAATTCCTTGGTAGT
TTGTCCTGAAACCCTACTGGAGAAGTCAGCATGAGGCACCTACTGAGAGAAGTGCCCAGA
AACTGCTGACTGCATCTGTTAAGAGTTAACAGTAAAGAGGTAGAAGTGTGTTTCTGAATCA
GAGTGGAAGCGTCTCAAGGGTCCCACAGTGAGGTCCCTGAGCTACCTCCCTTCCGTGAGT
GGGAAGAGTGAAGCCCATGAAGAACTGAGATGAAGCAAGGATGGGGTTCCTGGGCTCCA
GGCAAGGGCTGTGCTCTCTGCAGCAGGGAGCCCCACGAGTCAGAAGAAAAGAACTAATCA
TTTGTTGCAAGAAACCTTGCCCGGATACTAGCGGAAAACTGGAGGCGGNGGTGGGGGCAC
AGGAAAGTGGAAGTGATTTGATGGAGAGAGAAGCCTATGCACAGTGGCCCGAGTCCAC
TTGTAAAGTG

### 13728.132

## 13731.1&2

TGTGCCAGTCTACAGGCCTATCAGCAGCGACTCCTTCAGCAACAGATGGGGTCCCCTGTTC
AGGCCAACCCCATGAGCCCCCAGCAGCATATGCTCCCAAATCAGGCCCAGTCCCCACACCT
ACAAGGCCAGCAGATCCCTAATTCTCTCTCCAATCAAGTGCGCTCTCCCCAGCCTGTCCCTT
CTCCACGGCCACAGTCCCAGCCCCCCCACTCCAGTCCTTCCCCAAGGATGCAGCCTCAGCC
TTCTCCACACCACGTTTCCCCACAGACAAGTTCCCCACACTCCTGGACTGGTAGTTGCCCAG
GCCAACCCCATGGAACAAGGGCATTTTGCCCAG

### 13734.1&2

### 13736.2

### 13744.2-13696.2

# 13~46.1&2-13720.1&2

#### 14347.1

CAGATITITATITIGCAGTCGTCACTGGGGCCGTTTCTTGCTGCTTATITIGTCTGCTAGCCTG
CTCTTCCAGCTGCATGGCCAGGCGCAAGGCCTTGATGACATCTCGCAGGGCTGAGAAATGC
TTGGCTTGCTGGGCCAGAGCAGATTCCGCTTTGTTCACAAAGGTCTCCAGGTCATAGTCTG
GCTGCTCGGTCATCTCAGAGAGCTCAAGCCAGTCTGGTCCTTGCTGTATGATCTCCTTGAG
CTCTTCCATAGCCTTCTCCTCCAGCTCCCTGATCTGAGTCATGGCTTCGTTAAAGCTTGACA
TCTGGGAAGACAGTTCCTCCTTCCTTCGATAAATTGCCTGGAATCAGCGCCCCGTTAGA
GCAGGCTTCCATCTCTTCTTTTCCATTTGAATCAACTGCTCTCCACTGGGCCCACTGTGGG
GGCTCAGCTCCTTTGACCCTGCATATCTTAAGGGTGTTTAAAGGATATTCACAGGAGCT
TATGCCTGGT

### 14347.2

## 14348.2&14350.1&2

TCCCGAATTCAAGCGACAAATTGGAWAGTGAAATGGAAGATGCCTATCATGAACATCAGG CAAATCTTTTGCGCCAAGATCTGATGAGACGACAGGAAGAATTAAGACGCATGGAAGAAC TTCACAATCAAGAAATGCAGAAACGTAAAGAAATGCAATTGAGGCAAGAGGAGGACGA CGTAGAAGAGAGGAAGATGATGATTCGTCAACGTGAGATGGAAGAACAAATGAGGCG CCAAAGAGAGGAAAGTTACAGCCGAATGGGCTACATGGATCCACGGGAAAGAGACATGC GAATGGGTGGCGGAGGAGCAATGAACATGGGAGATCCCTATGGTTCAGGAGGCCAGAAA TTTCCACCTCTAGGAGGTGGTGGCATAGGTTATGAAGCTAATCCTGGCGTTCCACCAG CAACCATGAGTGGTTCCATGATGGGAAGTGACATGCGTACTGAGCGCTTTTGGGCAGGAG GTGCGGGGCCTTTGGGCACAGGGTCCTAGAGGAATGGGGCCTTTGGGCAGGAG ATGGTAGAGGGAGAGAGAGTACGAAGGC

## 14349.1&2

## 14352.1&2

GCGCGGGTGCGTGGGCCACTGGGTGACCGACTTAGCCTGGCCAGACTCTCAGCACCTGGA
AGCGCCCCGAGAGTGACAGCGTGAGGCTGGGAGGAGGACTTTGGCTTGAGCTTGTTAAAC
TCTGCTCTGAGCCTCCTTGTCGCCTGCATTTAGATGGCTCCCGCAAAGAAGGGTGGCGAGA
AGAAAAAGGGCCGTTCTGCCATCAACGAAGTCGTAACCCGAGAATACACCATCAACATTC
ACAAGCGCATCCATGGAGTGGGCTTCAAGAAGCGTGCACCTCGGGCACTCAAAGAGATTC
GGAAATTTGCCATGAAGGAGATGGGAACTCCAGATGTGCGCATTGACACCAGGCTCAACA
AAGCTGTCTGGGCCAAAGGAATAAGGAATGTGCCATACCGAATCCGTGTGCGGCTCCA
GAAAACGTAATGAGGATGAAGATTCACCAAATAAGCTATATACTTTGGTTACCTATGTACC
TGTTACCACTTTCAAAAATCTACAGACAGTCAATGTGGGATGAGAACTAATCGCTGATCGT

#### 14353.1

### 14353.2

## 17182.132

### 17183.2

GGTTCACAGCACTGCTGCTTGTGTGTTGCCGGCCAGGAATTCCAGGCTCACAAGGCTATCT
TAGCAGCTCGTTCTCCGGTTTTTAGTGCCATGTTTGAACATGAAATGGAGGAGAGCAAAAA
GAATCGAGTTGAAATCAATGATGTGGAGCCTGAAGTTTTTAAGGAAATGATGTGCTTCATT
TACACGGGGAAGGCTCCAAACCTCGACAAAATGGCTGATGATTTGCTGGCAGCTGCTGAC
AAGTATGCCCTGGAGCGCTTAAAGGTCATGTGTGAGGATGCCCTCTGCAGTAACCTGTCCG
TGGAGAACGCTGCAGAAATTCTCATCCTGGCCGACCTCCACAGTGCAGATCAGTTGAAAA
CTCAGGCAGTGGATTTCATCAACTATCATGCTTCGGATGTCTTGGAGACCTCTTGGG

## 17136.1&2

### 17137.132

## 1-191.1389.1

GGGGGTAGGCTCTTTATTAGACGGTTATT.GCTGTACTACAGGGTCAGAGTGCAGTGTAAGC
AGTGTCAGAGGCCCCGGTTCAGCCCAAGAATGTGGATTTTCTCTCCCTATTGATCACAGTG
GGTGGGTTTCTTCAGAAAAGCCCCAGAGGCAGGGACCAGTGAGCTCCAAGGTTAGAAGTG
GAACTGGAAGGCTTCAGTCACATGCTGCTTCCACGCTTCCAGGCTGGCAGCAAGGAGGA
GATGCCCATGACGTGCCAGGTCTCCCCCATCTGACACCAGTGAAGTCTGGTAGGACAGCAG
CCGCACGCCTGCCTCTGCCAGGAGGCCAATCATGGTAGGCAGCATTGCAGGGTCAGAGGT
CTGAGTCCGGAATAGGAGCAGGGCCAGTCCCTGCGGAGAGGCACTTCTGGCCTGAAGAC
AGCTCCATTGAGCCCCTGCAGTACAGGYGTAGTGCCTTGGACCAAGCCCACAGCCTGGTA
AGGGGCGCCTGCCAGGACGCCACGGCCAGGCCCA

## 17192.1&2

### 17193

AAGCGGATGGACCTGAGTCAGCCGGAATCCTAGCCCCTTCCCTTGGGCCTGCTGTGGTGCTC **G**ACATCAGTGACAGACGGAAGCAGCAGCATCAAGGCTACGGGAGGCCCGGGGGCGCTT GCGAAGATGAAGTTTGGCTGCCTCTCTTCCGGCAGCCTTATGCTGGCTTTGTCTTAAATG TCGCCGTCCACATTGCTCACAGGGGACTGGGGAAGGCGATGCCTGTCGGGGAGCTGCTGGTGG AGAGACTCGGGATGACTCCTGCTCAGATTCAGGCCTTGCTCAGGAAAGGGGGAAAAGTTTG GTCGAGGAGTGATAGCGGGACTCGFTGACATTGGGGGAAACTTTGCAATGCCCCGAAGACT TAACTCCCGATGAGGTTGTGGAACTAGAAAATCAAGCTGCACTGACCAACCTGAAGCAGA AGTACCTGACTGTGATTTCAAACCCCAGGTGGTTACTGGAGCCCATACCT.\$GGAAAGGAG GCAAGGATGTATTCCAGGTAGACATGCCAGAGCACCTGATCCCTTTGGGGCATGAAGTGT GACAAGTGTGGGCTCCTGAAAGGAATGTTCCRGAGAAACCAGCTAAATCATGGCACCTTC AATTTGCCATCGTGACGCAGACCTGTATAAATTAGGTTAAAGATGAATTTCCACTGCTTTG GAGAGTCCCACCCACTAAGCACTGTGCATGTAAACAGGTTCCTTTGCTCAGATGAAGGAA GTAGGGGGTGGGGCTT.TCCTTGTGTGATGCCTCCTTAGGCACACACGCAATGTCTCAAGTA CTT:GACCTTAGGGTAGAAGGCAAAGCTGCCAGTAAATGTCTCAGCATTGCTGCTAATTTT GGTCCTGCTAGTTTCTGGATTGTACAAATAAATGTGTTGTAGATGA

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## 16443.1.edit

TCGAGCGGCCGCCGGGCAGGTGTCGGAGTCCAGCACGGGAGGCGTGGTCTTGTAGTTGT
TCTCCGGCTGCCCATTGCTCTCCCACTCCACGGCGATGTCGCTGGGATAGAAGCCTTTGAC
CAGGCAGGTCAGGCTGACCTGGTTCTTGGTCATCTCCTCCCGGGATGGGGGCAGGGTGTAC
ACCTGTGGTTCTCGGGGCTGCCCTTTGGCTTTTCGAGATGGTTTTCTCGATGGGGGCTGGGA
GGGCTTTGTTTGGAGACCTTGCACTTGTACTCCTTGCCATTCAACCAGTCCTGGTGCANGAC
GGTGAGGACGCTNACCACACGGTACGNGCTGGTGTACTGCTCCTCCCGCGGCTTTGTCTTG
GCATTATGCACCTCCACGCCGTCCACGTACCAATTGAACTTGACCTCAGGGTCTTCGTGGC
TCACGTCCACCACCACGCATGTAACCTCAAANCTCCGGNCGCGANCACGC

## 16443.2.edit

## 16444.2.edit

## 16445.1.edir

## 16445.2.edit

### 16-146-1.edit

TCGAGCGGCCGCCCGGGCAGGTCCTCCTCAGAGCGGTAGCTGTTCTTATTGCCCCGGCAGC CTCCATAGATNAAGTTATTGCANGAGTTCCTCTCCACGTCAAAGTACCAGCGTGGGAAGG ATGCACGGCAAGGCCCAGTGACTGCGTTGGCGGTGCAGTATTCTTCATAGTTGAACATATC GCTGGAGTGGACTTCAGAATCCTGCCTTCTGGGAGCACTTGGGACAGAGGAATCCGCTGC ATTCCTGCTGGTGGACCTCGGCCGCGACCACGCT

## 16446.2.edit

AGCGTGGTCGCGGCCGAGGTCCACCAGCAGGAATGCAGCGGATTCCTCTGTCCCAAGTGC
TCCCAGAAGGCAGGATTCTGAAGACCACTCCAGCGATATGTTCAACTATGAAGAATACTG
CACCGCCAACGCAGTCACTGGGCCTTGCCGTGCATCCTTCCCACGCTGGTACTTTGACGTG
GAGAGGAACTCCTGCAATAACTTCATCTATGGAGGCTGCCGGGGCAATAAGAACAGCTAC
CGCTCTGAGGAGGACCTGCCCGGGGCGCCCCTCGA

## 16447.1.edic

### 16447.2.edit

### 16449.1.edit

AGCGTGGTCGCGGCCGAGGTCCTGTCAGAGTGGCACTGGTAGAAGNTCCAGGAACCCTGA
ACTGTAAGGGTTCTTCATCAGTGCCAACAGGATGACATGAAATGATGTACTCAGAAGTGTC
CTGNAATGGGGCCCATGANATGGTTGNCTGAGAGAGAGGCTTCTTGTCCTACATTCGGCGG
GTATGGTCTTGGCCTATGCCTTATGGGGGGTGGCCGTTGNGGGCGGTGNGGTCCGCCTAAAA
CCATGTTCCTCAAAGATCATTTGTTGCCCAACACTGGGTTGCTGACCANAAGTGCCAGGAA
GCTGAATACCATTTCCAGTGTCATACCCAGGGTGGGTGACGAAAGGGGTCTTTTGAACTGT
GGAAGGAACATCCAAGATCTCTGNTCCATGAAGATTGGGGTGTGGAAGGGTTACCAGTTG
GGGAAGCTCGCTGTTTTTCCTTCCAATCANGGGCTCGCTCTTCTGAATATTCTTCAGGGC
AATGACATAAATTGTATATTCGGTTCCCAGTCCAGGCCAG

### 16450.1.edic

## 16450.2.edir

AGCGTGGTCGCGGGGGAGGTCCTGTCAGAGTGGCACTGGTAGAAGTTCCAGGAACCCTGA
ACTGTAAGGGTTCTTCATCAGTGCCAACAGGATGACATGAAATGATGTACTCAGAAGTGTC
CTGGAATGGGGCCCATGAGATGGTTGTCTGAGAGAGAGGGTTTCTTGTCCTACATTCGGCGGG
TATGGTCTTGGCCTATGCCTTATGGGGGTGGCCGTTGTGGGCGGTGTGGTCCGCCTAAAAC
CATGTTCCTCAAAGATCATTTGTTGCCCAACACTGGGTTGCTGACCAGAAGTGCCAGGAAG
CTGAATACCATTTCCAGTGTCATACCCAGGGTGGTGACGAAAGGGGTCTTTTGAACTGTG
GAAGGAACATCCAAGATCTCTGGTCCATGAAGATTGGGGTTGTGGAAGGGTTACCAGTTGG
GGAAGCTCGTCTTTTTCCTTCCAATCANGGGCTCGCTCTTCTGATTATTCTTCAGGGC
AATGACATAAATTGTATATTCGGCTCCCGGGTNCAGCCAATAATAATAACCCTCTGTGACA
CCANGGCGGGGCCGAAGGANCACT

## 16451.2.edit

## 16451.1.edic

AGCGTGGCCGCGGCCGAGGTCCA.TGGCTGGAACGGCATCAACTTGGAAGCCAGTGATCG
TCTCAGCCTTGGTTCTCCAGCTAATGGTGATGGTGTCTCAGTAGCATCTGTCACACGAGC
CCTTCTTGGTGGGCTGACATTCTCCAGAGTGGTGACAACACCCTGAGCTGGTCTGCTTGTC
AAAGTGTCCTTAAGA 3CATAGACACTCACTTCATATTTGGCGNCCACCATAAGTCCTGATA
CAACCACGGAATGACCTGCAGGAAC

## 16452.Z.edic

### 16453.2.edit

## 16454.1.edit

AGCGTGGNTGCGGACGACGCCACAAAGCCATTGTATGTAGTTTTANTTCAGCTGCAAAN AATACCNCCAGCATCCACCTTACTAACCAGCATATGCAGACA

## 16454,2.edit

TCGAGCGGTCGCCCGGGCAGGTCTGGGCGGATAGCACCGGGCATATTTTGGAATGATGA GGTCTGGCACCCTGAGCAGCCCAGCGACTGGTCTTAGTTGAGCAATTTGGCTAGGA GGATAGTATGCAGCACGGTTCTGAGTCTGTGGGATAGCTGCCATGAAGNAACCTGAAGGA GGCGCTGGCTGGTANGGGTTGATTACAGGGCTGGGAACAGCTCGTACACTTGCCATTCTCT GCATATACTGGNTAGTGAGGCGAGCCTGGCGCTCTTCTTTGCGCTGAGCTAAAGCTACATA CAATGGCTTTGNGGACCTCGGCCGCGACCACGCTT 61 / 92

# 16455.1.edit

# 16455.2 edit

AGCGTGGTTTGCGGCCGAGGTCCTCACCANAGGTGCCACCTACAACATCATAGTGGAGGC ACTGAAAGACCAGCAGAGGCATAAGGTTCGGGAAGAGGTTGTTACCGTGGGCAACTCTGT CAACGAAGGCTTGAACCAACCTACGGATGACTCGTGCTTTGACCCCTACACAGNTTCCCAT TATGCCGTTGGAGATGAGTGGGAACGAATGTCTGAATCAGGCTTTAAACTGTTGTGCCAGT GCTTANGCTTTGGAAGTGGTCATTCAGATGTGATCATCTANATGGTGTCATGACAATGG TGNGAACTACAAGATTGGAAGAGTGGNACCGTCAGGGGANAAAATGGACCTGCCCGG GCGCNCGCTCGA

## 16456.1.edit

AGCGTGGTCGCCCGAGGTCTGGCTTNCTGCTCANGTGATTATCCTGAACCATCCAGGCCAAATAAAGCGCCGGCTATGCCCGTGNATTGGATTGCCACACGGCTCACATTGCATGCAAGTT

## 16456.2.edic

TCGAGCGGCCGCCGGGCAGGTCCAATTGAAACAACAGTTCTGAGACCGTTCTTCCACCA CTGATTAAGAGTGGCGNGGCGGGTATTAGGGATAATATTCATTTAGCCTTCTGAGCTTTCT GGGCAGACTTGGTGACCTTGCCAGCTCCAGCAGCCTTCTGGTCCACTGCTTTGATGACACC CACCGCAACTGTCTGTCTCATATCACGAACAGCGACCCAAAGGTGGATAGTCTGA GAAGCTCTCAACACACACTGGGCTTGCCAGGAACCATATCAACAATGGGCAGCATCACCAG ACTTCAAGAATTTAAGGGCCATCTTCCAGCTTTTTACCAGAACGGCGATCAATCTTTTCCTT

## 16459,2.edit

### 16460.1.edic

## 16460.2.edit

AGCGTGGTCGCGGCCGAGGTCCACATCGGCAGGGTCGGAGCCCTGGCCGCCATACTCGAA CTGGAATCCATCGGTCATGCTCTCGCCGAACCAGACATGCCTCTTGTCCTTGGGGTTCTTGC TGATGTACCAGTTCTTCTGGGGCCACACTGGGCTGAGTGGGGTACACGCAGGTCTCACCAGT CTCCATGTTGCAGAAGACTTTGATGGCATCCAGGNTGCAACCTTGGTTGGGGTCAATCCAG TACTCTCCACTCTTCCAGCCAGAGTGGCACATCTTGAGGTCACGGCAGGTGCGGNCGGGGG NTTTTGCGGCTGCCCTCTGGNCTTCGGNTGTNCTCNATCTGCTGGCTCA

## 16461.2.edit

## 16463.1.edit

AGCGTGGNNGCGGCCGAGGTATAAATATCCAGNCCATATCCTCCCTCCACACGCTGANAG ATGAAGCTGTNCAAAGATCTCAGGGTGGANAAAACCAT

## 16463.2.edit

CGAGCGGGCGACCGGGCAGGTNCAGACTCCAATCCANANAACCATCAAGCCAGATGTCAG
AAGCTACACCATCACAGGTTTACAACCAGGCACTGACTACAAGANCTACCTGCACACCTTG
AATGACAATGCTCGGAGCTCCCCTGTGGTCATCGACGCCTCCACTGCCATTGATGCACCAT
CCAACCTGCGTTTCCTGGCCACCACACCCCAATTCCTTGCTGGTATCATGGCAGCCGCCACG
TGCCAGGATTACCGGTACATCATCNAGTATGANAAGCCTGGGCCTCCTCCCAGAGAAGNG
GTCCCTCGGCCCCCGCCCTGNTGTCCCANAGGNTACTATTACTGNGCCNGCAACCGGCAACC
GATATCNATTTTGNCATTGGCCTTCAACAATAATTA

### 16464.Z.edit

## 16465.1.edit

AGCGTGGNCGCGGCCGAGGTGCAGCGCGGGCTGTGCCACCTTCTGCTCTCTGCCCAACGAT AAGGAGGGTNCCTGCCCCAGGAGAACATTAACTNTCCCCAGCTCGGCCTCTGCCGG

## 16465.2.edit

TCGAGCGGCCGGGGCAGGTTTTTTTGGTGAAAGTGGNTACTTTATTGGNTGGGAAAG GGAGAAGCTGTGGTCAGCCCAAAGAGGGAATACAGAGNCCCGAAAAAAGGGGAAGGCAGGT GGGCTGGAACCAGACGCAGGGCCAGGCAGAAACTTTCTCTCCTCACTGCTCAGCCTGGTG GTGGCTGGAGCTCANAAATTGGGAGTGACACAGGACACCTTCCCACAGCCATTGCGGCGG CATTTCATCTGGCCAGGACACTGGCTGTCCACCTGGTCCGGACAGAAAGCCCGAGC TGGGGAAAGTTAATGTTCACCTGGGGGCAGGAACCCTCCTTATCATTGNGCAGAGAGCAG AAGGTGGCACAGCCCGCGCTCCACCTCGGCCGCCCCCCT

## 16466.2.edir

TCGAGCGGCCGGGCAGGTCCACCATAAGTCCTGATACAACCACGGATGAGCTGTCA GGAGCAAGGTTGATTTCTTTCATTGGTCCGGNCTTCTCCTTGGGGGNCACCCGCACTCGAT ATCCAGTGAGCTGAACATTGGGTGGCGTCCACTGGGCCGCTCAGGCT

## 1646".2.edit

TCGAGCGGTTCGCCCGGGCAGGTCCACCACACCCAATTCCTTGCTGGTATCATGGCAGCCGCCACGTGCCAGGATTACCGGCTACATCATCAAGTATGAGAAGCCTGGGTCTCCTCCCAGAGAAGCGGTCCCTCGGCCCCGGCCCTGGTGTCACAGAGGCTACTATTACTGGCCTGGAACCGGGAACCGGGAACATATACAATTTATGTCATTGNCCTGAAGAATAATCANNAANAGCGANCCCCTGATTGGAAGGA

WO 00/36107 PCT/US99/30270

# 01\_16469.edit

# 

## 02\_16469.edit

TCGAGCGGNCGCCCGGGCAGGTCTGCCAACACCCAAGATTGGCCCCCGCCGCATCCACACA GTCCGTGTGCGGGGAGGT.AAC.AAGAAAT.ACCGTGCCCTGAGGTTGGACGTGGGGAATTTC TCCTGGGGCTCAGAGTGTTGTACTCGT.AAAACAAGGATCATCGATGTTGTCTACAATGCAT CTAATAACGAGCTGGTTCGTACCAAGACCCTGGTGAAGAATTGCATCGTGCTCATCGACAG CACACCGTACCGACAGTGGTACGAGTCCCACTATGCGCTGCCCCTGGGCCGCAAGAAGGG AGCCAAGCTGACTCCTGAGGAAGAAGAGATTTTAAACAAAAAACGATCTAANAAAAAA AAACAAT

# 03\_16470.edit

AGCGTGGTCGCGGCCGAGGTGAAATGGTATTCAGCTTCCTGGCACTTCTGGTCAGCAACCC ACGGCCACCCCATAAGGCATAGGCCAAGACCATACCCGCCGAATGTAGGACAAGAAGCT CTCTCTCAGACAACCATCTCATGGGCCCCATTCCAGGACACTTCTGAGTACATCATTTCATG TCATCCTGTTGGCACTGATGAAGAACCCTTACAGTTCAGGGTTCCTGGAACTTCTACCAGT GCCACTCTGACAGGACCTGCCCGGGCCGGCCGCTCGA

# 04\_16470.edit

TCGAGCGGCCGCGCGGGCAGGTCCTGTCAGAGTGGCACTGGTAGAAGTTCCAGGAACCCT GGGTATGGTCTTGGCCTATGCCTTATGGGGGGTGTGGCCGTTGTGGGCGGTGTGGTCCGCCTAA AACCATGTTCCTCAAAGATCATTTGTTGCCCAACACTGGGTTGCTGACCAGAAGTGCCAGG AAGCTGAATACCATTTCACCTCGGCCGCGACCACGCTA

# 05\_16471.edit

TCGAGCGGCCGCCCGGGCAGGTCTCCCTTCTTGCGGCCCAGGGGCAGCGCATAGTGGGAC TCGTACCACTGTCGGTACGGTGTGCTGTCGATGAGCACGATGCAATTCTTCACCAGGGTCT TGGTACGAACCAGCTCGTTATTAGATGCATTGTAGACAACATCGATGATCCTTGTTTTACG AGTACAACACTCTGAGCCCCAGGAGAAATTCCCCAACGTCCAACCTCAGGGCACGGTATTTC TTGTTACCTCCCGCACACGGACTGTGTGGATGCGGCGGGGGCCAAGCTGACTCCTGAGGA AGAAGAGATTTTAAACAAAAACGATCTAAAAAAATTTCAGAAGAAATATGATGAAAGGA AAAAGAATGCCAAAATCAGCAGTCTCCTGGAGGAGCAGTTCCAGCAGGGCAAGCTTCTTG CGTGCATCGCTTCAAGGCCGGGACAGTGTGACCGAGCAGATGGCTATGTGCTAGAGGGCA AAGAAGTGGAGTTCTATCTTAAGAAAATCAGGGCCCAGAATGGTGNGTCTTCAACTAATC CAAAGGGGAGTTTCAGACCAGTGCAATCAGCAAAAACATTGATACTGNTGGCCAAATTTA TTGGTGCAGGGCTTGCACANTANGANNGGCTGGGTCTTGGGGGCTTGGATTGGNACAAGCT TTGGCAGCCTTTTCTTTGGTTTTGCCAAAAACCTTTGNTGAAGANGANACCTNGGGCGGA CCCCTTAACCGATTCCACNCCNGGNGGCGTTCTANGGNCCCNCTTG

# 06\_16471.edit

# 07\_16472\_edit

TCGAGCGGCCGCCGGGCAGGTCCCCAACCAAGGCTGCAACCTGGATGCCATCAAAGTCT TCTGCAACATGGAGACTGGTGAGACCTGCGTGTACCCCACTCAGCCCAGTGTGGCCCAGA AGAACTGGTACATCAGCAAGCACCCCAAGGACAAGAGGCATGTCTGGTTCGGCGAGAGCA TGACCGATGGATTCCAGTTCGAGTATGGCGGCCAGGGCTCCGACCCTGCCGATGTGGACCT CGGCCGCGACCACGCT

# 08\_16472.edit

# 09\_16473.edit

# 11\_16474.edit

# 12\_16474.edit

# 13\_16475.edit

## 14\_16475.edit

# 15\_16476.edit

## 16\_16476.edit

# 17\_16477.edit

# 18\_16477.edit

# 21\_16479.edit

# 22\_16479.edit

## 24\_16480.edit

TCGAGCGNNCGCCCGGGCAGGTCCAGTAGTGCCTTCGGGACTGGGTTCACCCCCAGGTCTG
CGGCAGTTGTĈACAGCGCCAGCCCGCTGGCCTCCAAAGCATGTGCAGGAGCAAATGGCA
CCGAGATATTCCTTCTGCCACTGTTCTCCTACGTGGTATGTCTTCCCATCATCGTAACACGT
TGCCTCATGAGGGTCACACTTGAATTCTCCTTTTCCGTTCCCAAGACATGTGCAGCTCATTT
GCCTCATGAGGTCACACTTGAATTCTCCTTTTCCGTTCCCAAGACATGTGCAGCTCATTT
TCTCTACTGGAGCTTTCGTACCTTCCACTTCTGCTGTTGGTAAAATGGTGGATCTTCTATCA
ATTTCATTGACAGTACCCACTTCTCCCAAACATCCAGGGAAATAGTGATTTCAGAGCGATT
AGGAGAACCAAATTATGGGGCAGAAATAAGGGGCTTTTCCACAGGTTTTCCTTTTGGAGGA
AGATTTCAGTGGTGACTTTAAAAGAATACTCAACAGTGTCTTCATCCCCATAGCAAAAGAA
GAAACNGTAAATGATGGAANGCTTCTGGAGATGCCNNCATTTAAGGGACNCCCAGAACTT
CACCATCTACAGGACCTACTTCAGTTTACANNAAGNCACATANTCTGACTCANAAAGGAC
CCAAGTAGCNCCATGGNCAGCACTTTNAGCCTTTCCCCTGGGGAAAANNTTACNTTCTTAA
ANCCTNGGCCNNGACCCCCTTAAGNCCAAATTNTGGAAAAANTTCCNTNCNNCTGGGGGGC
NGTTCNACATGCNTTTNAAGGGCCCCAATTNCCCCNT

# 25\_16481.edit

TCGAGCGGCCGCGGGCAGGTGTCGGAGTCCAGCACGGGAGGCGTGGTCTTGTAGTTGT
TCTCCGGCTGCCCATTGCTCTCCCACTCCACGGCGATGTCGCTGGGATAGAAGCCTTTGAC
CAGGCAGGTCAGGCTGACCTGGTTCTTGGTCATCTCCTCCCGGGATGGGGGCAGGGTGTAC
ACCTGTGGTTCTCGGGGCTGCCCTTTGGCTTTTGGAGATGGTTTTCTCGATGGGGGCTGGGA
GGGCTTTGTTGGAGACCTTGCACTTGTACTCCTTGCCATTCAGCCAGTCCTGGTGCAGGAC
GGTGAGGACGCTGACCACACGGGTACGTGTTGTACTGCTCCTCCCGCGGGCTTTGTCTTG
GCATTATGCACCTCCACGCCGTCCACGTACCAGTTGAACTTGACCTCAGGGTCTTCGTGC
TCACGTCCACCACCCACGCATGTAACCTCAGACCTCGGCCGCACCACGCT

## 25\_16481.edit

# 27\_16482.edit

TCGAGCGGCCGCGGGCAGGTTGAATGGCTCCTCGCTGACCACCCCGGTGCTGGTGGTGG GTACAGAGCTCCGATGGGTGAAACCATTGACATAGAGACTGTCCCTGTCCAGGGTGTAGG GGCCCAGCTCAGTGATGCCGTGGGTCAGCTGGCTCAGCTTCCAGTACAGCCGCTCTCTGTC CAGTCCAGGGCTTTTGGGGTCAGGACGATGGGTGCAGACAGCATCCACTCTGGTGGCTGC CCCATCCTTCTCAGGCCTGAGCAAGGTCAGTCTGCAACCAGAGTACAGAGAGCTGACACT GGTGTTCTTGAACAAGGGCATAAGCAGACCCTGAAGGACACCTCGGCCGCCGACCACGCT

## 23\_16482.edit

AGCGTGGTCGCGGCCGAGGTGTCCTTCAGGGTCTGCTTATGCCCTTGTTCAAGAACACCAG
TGTCAGCTCTCTGTACTCTGGTTGCAGACTGACCTTGCTCAGGCCTGAGAAGGATGGGGCA
GCCACCAGAGTGGATGCTGTCTGCACCCATCGTCCTGACCCCAAAAGCCCTGGACTGGACA
GAGAGCGGCTGTACTGGAAGCTGAGCCAGCTGACCCACGGCATCACTGAGCTGGGCCCCT
ACACCCTGGACAGGGACAGTCTCTATGTCAATGGTTTCACCCATCGGAGCTCTGTACCCAC
CACCAGCACCCGGGGTGGTCAGCGAGGACCCATTCAACCTGCCCGGGCGCCGCTCGA

# 29\_16483.edit

AGCGTGGTCGCGGCCGAGGTCCTGTCAGAGTGGCACTGGTAGAAGTTCCAGGAACCCTGA
ACTGTAAGGGTTCTTCATCAGTGCCAACAGGATGACATGAAATGATGTACTCAGAAGTGTC
CTGGAATGGGGCCCATGAGATGGTTGTCTGAGAGAGAGGCTTCTTGTCCTACATTCGGCGGG
TATGGTCTTGGCCTATGCCTTATGGGGGTGGCCGTTGTGGGCGGTGTGGTCCGCCTAAAAC
CATGTTCCTCAAAGATCATTTGTTGCCCAACACTGGGTTGCTGACCAGAAGTGCCAGGAAG
CTGAATACCATTTCCAGTGTCATACCCAGGGTGGGTGACGAAAGGGGTCTTTTGAACTGTG
GAAGGAACATCCAAGATCTCTGGTCCATGAAGATTGGGGTGTGGAAGGGTTACCAGTTGG
GGAAGCTCGTCTTTTTCCTTCCAATCAGGGGCTCGCTCTTCTGATTATTCTTCAGGGC
AATGACATAAATTGTATATTCGGTCCCGGTTCCAGGCCAGTAATAGTAGCCTCTTGTGACAC
CAGGGCGGGGCCGAGGGACCCCTTCTNTTGGAAGAGACCAGCTTCTCATACTTGATGATGA
GNCCGGTAATCCTGGCACGTGGNGGTTGCATGATNCCACCAAGGAAATNGGNGGGGGNG
GACCTGCCCGGCGGCCGGTTCNAAAGCCCAATTACTTGGNGGCCGTACTATGGATC
CCACTCNGTCCAACTTGGNGGAATATGGCATAACTTTT

# 31\_16484.edit

# 37\_16487.edit

AGCOTGGTCGCGGCCGAGGTCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTG GTGACCGTGCCCTCCAGCAACTTCGGCACCCAGACCTACACCTGCAACGTAGATCACAAGC CCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACAT GCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCGCAT CCCCCTTCCAAACCTGCCGGGGGGGCCGCTCG

# 38\_16487.edit

CGAGCGGCCGCCGGGCAGGTTTGGAAGGGGGATGCGGGGGAAGAGAGACTGACGGT CCCCCCAGGAĞTTCAGGTGCTGGGCACGGTGGGCATGTGTGAGTTTTGTCACAAGATTTGG GCTCAACTCTCTTGTCCACCTTGGTGTTGCTGGGCTTGTGATCTACGTTGCAGGTGTAGGTC TGGGTGCCGAAGTTGCTGGAGGGCACGGTCACCACGCTGCTGAGGGGAGTAGAGTCCTGAG GACTGTAGGACAGACCTCGGCCGCCGACCACGCT

# 39\_16488.edit

NGGNNGGTCCGGNCNGNCAGGACCACTCNTCTTCGAAATA

# 41\_16489.edit

AGCGTGGTCGCGGCCGAGGTCCTCACTTGCCTCCTGCAAAGCACCGATAGCTGCGCTCTGG AAGCGCAGATCTGTTTTAAAGTCCTGAGCAATTTCTCGCACCAGACGCTGGAAGGGAAGTT TGCGAATCAGAAGTTCAGTGGACTTCTGATAACGTCTAATTTCACGGAGCGCCACAGTACC AGGACCTGCCCGGGCGGCCGCTCGA

# 42\_16489.edit

# 45\_16491.edic

73 / 92

# 46\_16491.edit

# 47\_16492.edit

# 48\_16492.edit

# 49\_16493.edit

# 55\_16496.edit

AGCGTGGTCGCGGCCGAGGTCCTCACCAGAGGTGCCACCTACAACATCATAGTGGAGGCA CTGAAAGACCAGCAGAGGCATAAGGTTCGGGAAGAGGTTGTTACCGTGGGCAACTCTGTC AACGAAGGCTTGAACCAACCTACGGATGACTCGTGCTTTGACCCCTACACAGTTTCCCATT ATGCCGTTGGAGATGAGTGGGAACGAATGTCTGAATCAGGCTTTAAACTGTTGTGCCAGTG CTTAGGCTTTGGAAGTGGTCATTTCAGATGTGATCATCTAGATGGTGCCATGACAATGGT GTGAACTACAAGATTGGAGAGAAGTGGGACCGTCAGGGAGAAAATGGACCTGCCCGGGC

# 56\_16496.edit

# 59\_16498.edit

TCGAGCGGCCGCCGGGCAGGTCCACCATAAGTCCTGATACAACCACGGATGAGCTGTCA
GGAGCAAGGTTGATTTCTTTCATTGGTCCGGTCTCTCTTTGGGGGTCACCCGCACTCGATA
TCCAGTGAGCTGAACATTGGGTGGTGTCCACTGGGCGCTCAGGCTTGTGGGTGTGACCTGA
GTGAACTTCAGGTCAGTTGGTGCAGGAATAGTGGTTACTGCAGTCTGAACCAGAGGCTGA
CTCTCCCGCTTGGATTCTGAGCATAGACACTAACCACATACTCCACTGTGGGCTGCAAGC
CTTCAATAGTCATTTCTGTTTGATCTGGACCTGCAGTTTTAGTTTTTGTTGGTCCTGGTCCAT
TTTTGGGAGTGGTGATCTCTGTAACCAGTAACAGGGGAACTTGAAGGCAGCCACTTGAC
ACTAATGCTGTTGTCCTGAACATCGGTCACTTGCATCTGGGATGGTTTGNCAATTTCTGTTC
GGTAATTAATGGAAATTGGCTTGCTGCTT.GCGGGGGCTGTCTCCACGGCCAGTGACAGCATA
CACAGNGATGGNATNATCAACTCCAAGTTTAAGGCCCTGATGGTAACTTTAAACTTGCTCC
CAGCCAGNGAACTTCCGGGACAGGGTATTTCTTGTTC
CACGCCAGNGAACTTCCGGGACAGGGTATTTCTTGTTCCGAACAGNGANCCTGGGACATNN
TCTCCTTGGGANCAGAAGGANCNTCCAAAACTTGGGCCCGGAACCCCTT

## 60\_16473.edit

## 60\_16498.edit

61\_15499.±dit

AGCGTGGTCGCGGCCGAGGTCNAGGA

# 62\_16483.edit

# 63\_16500.edit

# 64\_16493.edit

## 64\_16500.edit

TCGAGCGGCCGCCGGGCAGGTCCTCACCAGAGGTGCCACCTACAACATCATAGTGGAGG CACTGAAAGACCAGCAGAGGCATAAGGTTCGGGAAGAGGTTGTTACCGTGGGCAACTCTG TCAACGAAGGCTTGAACCAACCTACGGATGACTCGTGCTTTGACCCCTACACAGTTTCCCA TTATGCCGTTGGAGATGAGTGGGAACGAATGTCTGAATCAGGCTTTAAACTGTTGTGCCAG TGCTTAGGCTTTGGAAGTGGGTCATTCAGATGTGATCATCTAGATGGTGCCATGACAATG GTGTGAACTACAAGATTGGAGAGAAGTGGGACCGTCAGGGAGAAAATGGACCTCGGCCG CGACCACGCT 77 / 92

### 16501.edit

## 16501.2.edit

GAGGACTGGCTCAGCTCCAGTATAGCCGCTCTCTGTCCAGTCCAGGACCAGTGGGATCAA GGCGGAGGGTGCAGATGGCGTCCACTCCAGTGGCTGCCCCATGTTTCTCAAGTCTGAGCAA AGNCAGTCTGCAGCCAGAGTACAGAGGGCCAACACTGGTGCTCTTGAACAGGGACCTGAG CAGGCCCTGAAGGACCCTCTCCGTGGTGTTGAACTTCCTGGAGCCAGGGTGCTGCATGTTC TCCTCATACCGCAGGTTGTTGATGGTGAAGTTCAGTGTGAATGGCTCCTCGCTGACCACCC

## 16502.1.edit

## 16502.2.edit

AGCGTGGNCGCGGCCGAGGTCTGAGGATGTAAACTCTTCCCAGGGGAAGGCTGAAGTGCTGACCATGGTGCTACTGGGTCCTTCTGAGTCAGATATGTGACTGATGNGAACTGAAGTAGGTACTGTAGATGGTGAAGTCTGAGTCCCTAAATGCTGCATCTCCAGAGCCTTCCATCATTACCGTTTCTTTTTTGCTATGGGATGAGACACTGTTGAGTATTCTCTAAAGTCACCACTGAAATCTCCCCCAAAGGAAAACCTGTGGAAAAGCCCCTTATTTCTGCCCCATAATTTGGTTCTCCTAATCNCTCTGAAATCACTATTTCCCTGGAANGTTTGGGAAAANNGGGCNACCTGNCANTGGAAANTGGATANAAAAGATCCCACCATTTTACCCAACNAGCAGAAAGTGGGAANGGTACCGAAAAGCTCCAAGTAANAAAAAGGAGGGGAAGTAAAAGGTCAAGTGGGCACCAGTTTCAAACCAAAACTTTCCCCAAACTATANAACCCA

## 16503.2.edit

AAGCGGCCGCCCGGGCAGGNNCAGNAGTGCCTTCGGGACTGGGNTCACCCCCAGGTCTGC
GGCAGITGTCACAGCGCCAGCCCCGCTGGCCTCCAAAGCATGTGCAGGAGCAAATGGCAC
CGAGATAITCCTTCTGCCACTGTTCTCCTACGTGGTAIGTCTTCCCATCATCGTAACACGTT
GCCTCATGAGGGTCACACTTGAATTCTCCTTTTCCGTTCCCAAGACATGTGCAGCTCATTTG
GCTGGCTCTATAGTTTGGGGAAAGTTTGTTGAAACTGTGCCACTGACCTTTACTTCCTCTT
CTCTACTGGAGCTTTCCGTACCTTCCACTTCTGCTGNTGGNAAAAAGGGNGGAACNTCTTA
TCAATTTCATTGGACAGTANCCCNCITTCTNCCCAAAACATNCAAGGGAAAATATTGATTN
CNAGAGCGGATTAAGGAACAACCCNAATTATGGGGGGCCAGAAATAAAAGGGGGGCTTTTCCA
CAGGTNTTTTCCT

## 16504.1.edi:

TCGAGCGGCCGGGCAGGTCTGCAGGCTATTGTAAGTGTTCTGAGCACATATGAGAT AACCTGGGCCAAGCTATGATGTTCGATACGTTAGGTGTATTAAATGCACTTTTGACTGCCA TCTCAGTGGATGACAGCCTTCTCACTGAGAGCAGAGATCTTCCTCACTGTGCCAGTGGGCA GGAGAAAGAGCATGCTGCGACTGGACCTCGGCCGCGACCACGCT

## 16504.2.edit

AGCGTGGTCGCGGCCGAGGTCCAGTCGCAGCATGCTCTTTCTCCTGCCCACTGGCACAGTG AGGAAGATCTCTGCTGTCAGTGAGAAGGCTGTCATCCACTGAGATGGCAGTCAAAAGTGC ATTTAATACACCTAACGTATCGAACATCATAGCTTGGCCCAGGTTATCTCATATGTGCTCA GAACACTTACAATAGCCTGCAGACCTGCCCGGGCGGCCGCTCGA

CGAGCGGCCGGGGCAGGTCCAGACTCCAATCCAGAGAACCACCAAGCCAGATGTCAG
AAGCTACACCATCACAGGTTTACAACCAGGCACTGACTACAAGATCTACCTGTACACCTTG
AATGACAATGCTCGGAGCTCCCCTGTGGTCATCGACGCCTCCACTGCCATTGATGCACCAT
CCAACCTGCGTTTCCTGGCCACCACACCCAATTCCTTGCTGGTATCATGGCAGCCGCCACG
TGCCAGGATTACCGGCTACATCATCAAGTATGAGAAGCCTGGGTCTCCTCCCAGAGAAGT
GGTCCCTCGGCCCCGCCCTGGTGNCACAGAAGCTACTATTACTGGCCTGGAACCGGGAACC
GAATATACAATTTATGTCATTGCCCTGAAGAATAATCANAAGAGCGAGCCCCTGATTGGA
AGG

## 16505.2.edit

AGCGTGGTCGCGGCCGAGGTCCTGTCAGAGTGGCACTGGTAGAAGTTCCAGGAACCCTGA
ACTGTAAGGGTTCTTCATCAGTGCCAACAGGATGACATGAAATGATGTACTCAGAAGTGTC
CTGGAATGGGGCCCATGAGATGTTGTCTGAGAGAGAGGGTTCTTGTCCTGTCTTTTTCCTTC
CAATCAGGGGCTCGCTCTTCTGATTATTCTTCAGGGCAATGACATAAATTGTATATTCGGTT
CCCGGTTCCAGGCCAGTAATAGTAGCCTCTGTGACACCAGGGCGGGGCCGAGGGACCACT
TCTCTGGGAGGAGCCCAGGCTTCTCATACTTGATGATGTANCCGGTAATCCTGGCACCGT
GGCGGCTGCCATGATACCAGCAAGGAATTGGGTTGGCCAAGAAACGCAGGTTGGAT
GGTGCATCAATGGCAGTGGAGGCGTCGATNACCACAGGGGAGCTCCGANCATTGTCATTC
AAGGTGGACAGGTAGAATCTTGTAATCAGGTGCCTGGTTTGTAAACCTG

### 16506.1.edic

TCGAGCGGCCGGCCGGGCAGGTTTCGTGACCGTGACCTCGAGGTGGACACCACCCTCAAG
AGCCTGAGCCAGCAGATCGAGAACATCGGGAGCCCAGAGGGCAGCCGCAAGAACCCCGC
CCGCACCTGCCGTGACCTCAAGATGTGCCACTCTGACTGGAAGAGTGGAGAGTACTGGAT
TGACCCCAACCAAGGCTGCAACCTGGATGCCATCAAAGTCTTCTGCAACATGGAGACTGGT
GAGACCTGCGTGTACCCCAACCTCAGCCCAGTGGGCCCAGAAGAACTGGTACATCAGCAAG
AACCCCAAGGACAAGAAGCATGTCTGGTTCGGCGCAAAGCATGGATGCATCCAGTTC
GAGTATGGCGGCCAGGGCTCCGACCTTGCCGATGGATCCCAGTTC
CCCGAATTCCAGCACACTGGCGGCCCTTACTAGTGGGATCCGAGCTTCCGTACCAAGCTTG
GCGTAATCATGGGNCATAGCTGTTTCCTGNGTGAAAATGGTATTCCGCTTCACAATTTCCC
AC

### 16506.2.edit

## 16507.2.edit

## 16508.1.edit

## 16508.2.edic

WO 00/36107 PCT/US99/30270

## 16509.1.edit

### 16509.2.edit

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TCCTTTAGGGCGATCAATGTTGGTTACTGCAGTCTGAACCAGAGGCTGACTCTCTCCGCTT
GGATTCTGAGCATAGACACTAACCACATACTCCACTGTGGGCTGCAAGCCTTCAATAGTCA
TTTCTGTTTGATCTGGACCTGCAGTTTTAAGTTTTTTGGTGGTCCTGNCCCATTTTTTGGAAG
TGGGGGGTTACTCTGTAACCAGTAACAGGGGAACTTGAAGGCAGCCACTTGACACTAATG
CTGTTGTCCTGAACATCGGTCACTTGCATCTGGGGATGGTTTTGACAATTTCTGGTTCGGCA
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CC

### 16510.1.edit

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GGGAATAGCTCATGGATTCCATCCTCAGGGCTCGAGTAGGTCACCTGTACCTGGAAACTT
GCCCTGTGGGCTTTCCCAAGCAATTTGATGGAATCGACATCCACATCAGTGAATGCCAG
TCCTTTAGGGGGATCAATGTTGGTTACTGCAGTCTGAACCAGAGGCTGACTCTCTCCGCTT
GGATTCTGAGCATAGACAACTAACCACATACCACATGTGGGCTGCAAGCCTTCAATAGTCA
TTTCTGTTTGATCTGGACCTGCAGTTTTAAGTTTTTGTTGGNCCTGNNCCATTTTTGGGGAA
GGGGTGGTTACTCTTGTAACCAGTAACAGGGGAACTTGAAGCAGCCACTTGACACTAATG
CTGGTGGCCTGAACATCGGGTCACTTGCATCTGGGATGGTCAATTTCTGTTCGGTAAT
TAATGGGAAATTGGCTTACTGGCTTGCGGGGGGCTGTCTCCACGGNCAGTGACAAGCATAC
ACAGGNGATGGGTATAATCAACTCCAGGTTTAAGGCCNCTGGTGA
ACAGGNGATGGGTATAATCAACTCCCAGGTTTAAGGCCNCTGGTGAT

## 16510.2.edit

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CCTCCCTCCGCGTCCGGGTCTCCTGGACAGTCAGTCACCATCTCCTGCACTGGAACCAGCA
GTGACGTTGGTGCTTATGAATTTGTCTCCTGGTACCAACACACCCCAGGCAAGGCCCCCAA
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AAGTCTGGCAACACGGCCTCCCTGACCGTCTCTGGGCTCCANGCTGAGGATGANGCTGATT
ATTACTGGAAGCTCATATGCAGGCAACAATTGGGTGTTCGGCGGAAGGGACCAAGCT
GACCGTNCTAAGGTCAAGCCCAAGGCTTGCCCCCCTCGGTCACTCTGTTCCCACCCTCCTCT
GAAGAAGCTTTCAAGCCCAACAANGNCACACTGGGTGTTCTCATAAGTGGACTTTCTACCC

## 16511.2.edit

#### 16512.1.edit

AGCGTGGTCGCGGCCGAGGTCCAGCATCAGGAGCCCCGCCTTGCCGGCTCTGGTCATCGCC
TTTCTTTTGTGGCCTGAAACGATGTCATCAATTCGCAGTAGCAGAACTGCCGTCTCCACTG
CTGTCTTATAAGTCTGCAGCTTCACAGCCAATGGCTCCCATATGCCCAGTTCCTTCATGTCC
ACCAAAGTACCCGTCTCACACATTTACACCCCAGGTCTCACAGTTCTCCTGGGTTGCTTGG
CCCGAAGGGAGGTAAGTANACGGATGGTGCTGGTCCCACAGTTCTCGGATCAGGGTACGAG
GAATGACCTCTAGGGCCTGGGCNACAAGCCCTGTATGGACCTGCCCGGGCGGGCCGGCCGGTC
GA

#### 16512.2.edit

TCGAGCGCCCCCGGGCAGGTCCATACAGGGCTGTTGCCCAGGCCCTAGAGGNCATTCC
TTGTACCCTGATCCAGAACTGTGGGACCAGGACCATCCGTCTACTTACCTCCCTTCGGGCC
AAGCACACCCAGGAGAACTGTGAGACCTGGGGTGTAAATGGNGAGACGGGTACTTTGGTG
GACATGAAGGAACTGGGCATATGGGAGCCATTGGCTGNGAAGCTGCANACTTATAAGACA
GCAGTGGAGACGGCAGTTCTGCTACTGCGAATTGATGACATCGTTTCAGGCCACAAAAAG
AAAGGCGATGACCANAGCCGGCAAGGCGGGGGTTCCTGATGCTGGACCTCGGCCGCCGAC
CACGCTT

AGCGTGGTCGCGGCCGAGGTCCACTAGAGGTCTGTGCCATTGCCCAGGCAGAGTCTCTG
CGTTACAAACTCCTAGGAGGGCTTGCTGTGCGGAGGGCCTGCTATGGTGTGCTGCGGTTCA
TCATGGAGAGTGGGGCCALAGGCTGCGAGGTTGTGGTGTCTGGGAAACTCCGAGGACAGA
GGGCTAAATCCATGAAGTTTGTGGATGGCCTGATGATCCACAGCGGAGACCCTGTTAACTA
CTACGTTGACACTGCTGTGCGCCACGTGTTGCTCANACAGGGTGTGCTGGGCATCAAGGTG
AAGATCATGCTGCCCTGGGACCCANCTGGCAAAAATGGCCCTTAAAAAACCCCTTGCCNTG
ACCACGTGAACCATTTGTGNGAACCCCAAGATGAANATACTTGCCCACCACCCCCCATTC

## 16514.2.edit

## 16515.1.edit

## 16515.Z.edit

TCGAGCGGCCCGGGCAGGTCTGGGCCAGGGGCACCAACACGTCCTCTCACCAGGA AGCCCACGGGCTCCTGTTTGACCTGGAGTTCCATTTTCACCAGGGGCACCAGGTTCACCCT TCACACCAGGAGCACCGGGCTGTCCCTTCAATCCATCCAGACCATTGTGNCCCCTAATGCC TTTGAAGCCAGGAAGTCCAGGAGTTCCAGGGAAACCACGAGCACCCTGTGGTCCAACAAC TCCTCTCACCAGGTCGTCCGGGGTTTTCCAGGGTGACCATCTTCACCAGCCTTGCCAGGA GGGCCAGACCTCGGCCGCGACCACCT

ANCGTGGTCGCGGCCGAGGTCCTCACCAGAGGTGNCACCTACAACATCATAGTGGAGGCACTGAAAGACGANCAGAGGCATAAGGTTCGGGAAGAGG

#### 16516.2.edit

#### 16517.1.edir

## 16518.1.edit

AGCGTGGTCGCGGCCGAGGTCTGAGGTTACATGCGTGGTGGTGGACGTGAGCCACGAAGA CCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAA GCCGCGGGGAGGAGCAGTACAACAACAACACAAACACCACGTACCGGGNGGTCAGCGTCCTCACCGTCCTGCA CCAGAATTGGTTGAATGGCAAGGAGTACAAGNGCAAGGTTTCCAACAAAGCCNTCCCAGC CCCCNTCGAAAAAAACCATTCCAAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACAC CCTGCCCCCATCCCGGGAGAAAAAAAACAATTCCCCCCNTCGAAAAACCAATTGCTTGGTC NAANGCTTTTATCCCAACGNACTTCCCCCCNTGGAANTGGGAAAAACCAATGGGCCAANC CGAAAAAACAATTACAANAACCCC

## 16513.2.edit

TCGAGCGGCCGCCCGGGCAGGTGTCGGAGTCCAGCACGGGAGGCGTGGTCTTGTAGTTGT
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CAGGCAGGTCAGGCTGACCTGGTTCTTGGTCATCTCCCGGGGATGGGGGCAGGGTGAA
CACCTGGGGTTCTCGGGGGCTTGCCCTTTGGTTTTGAANATGGTTTTCTCGATGGGGGCTGG
AAGGGCTTTGTTGNAAACCTTGCACTTGACTCCTTGCCATTCACCCAGNCCTGGNGCAGGA
CGGNGAGGACNCTNACCACACGGAACCGGGCTGGTGGACTGCTCC

AGCGTGGTCGCGGACGANGTCCTGTCAGAGTGGNACTGGTAGAAGTTCCANGAACCCTGA ACTGTAAGGGTTCTTCATCAGTGCCAACAGGATGACATGAAATGATGTACTCAGAAGNGN CCTGGAATGGGGCCCATGANATGGTTGCC

### 16519.2.edit

#### 16520.1.edit

#### 16520.2.edit

### 16521.2.edit

TCGAGCGGCCGCGGGCAGGTCTGGTGGGGTCCTGGCACACGCACATGGGGGNGTTGNT
CTNATCCAGCTGCCCAGCCCCCATTGGCGAGTTTGAGAAGGTGTGCAGCAATGACAACAA
NACCTTCGACTCTTCCTGCCACTTCTTTGCCACAAAGTGCACCCTGGAGGGCACCAAGAAG
GGCCACAAGCTCCACCTGGACTACATCGGGCCTTGCAAATACATCCCCCCTTGCCTGGACT
CTGAGCTGACCGAATTCCCCCCTTGCGCATGCGGGACTGGCTCAAGAACCGTCCTGGCACC
TTGTATGANAGGGATGAAGACACNACCC

AGCGTGGTCGCGGCCGAGGTCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTG
GTGACCGTGGCCTCCAGCAACTTCGGCACCCAGACCTACACCTGCAACGTAGATCACAAGC
CCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACAT
GCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCGCAT
CCCCCTTCCAAACCTGCCCGGGCGGCCGCTCGAAAGCCGAATTCCAGCACACTGGCGGCCG
GTACTAGTGGANCCNAACTTGGNANCCAACCTGGNGGAANTAATGGGCATAANCTGTTTC
TGGGGGGGAAATTGGTATCCNGTTTACAATTCCCNCACAACATACGAGCCGGAAGCATAAA
AGNGTAAAAGCCTGGGGGGNGGCCTANTGAAGTGAAGCTAAACTCACATTAATTNGCGTTG
CCGCTCACTGGCCCGCTTTTCCAGC

# 16522.2.edit

TCGAGCGGCCGCCCGGGCAGGTTTGGAAGGGGGATGCGGGGGAAGAGAGACTGACGG
TCCCCCAGGAGTTCAGGTGCTGGGCACGGTGGGCATGTGTGAGTTTTGTCACAAGATTTG
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CTGGGNGCCGAAGTTGCTGGAGGGCACGGTCACCACGCTGCTGAGGGAGTAGAGTCCTGA
GGACTGTANGACAGACCTCGGCCGNGACCACGCTAAGCCGAATTCTGCAGATATCCATCA
CACTGGCGGCCGCCCCGAGCATGCATTTTAGAGG

### 16523.1.edit

AGCGTGGNCGCGGACGANCACAACAACCCC

## 16523.2.edit

#### 16524.1.edit

AGCGTGGTCGCGGCCGAGGTCCAGCCTGGAGATAANGGTGAAGGTGGTGCCCCCGGACTT CCAGGTATAGCTGGACCTCGTGGTAGCCCTGGTGAGAGAGGTGAAACTGGCCCTCCAGGA CCTGCTGGTTTCCCTGGTGCTCCTGGACAGAATGGTGAACCTTGGNGGTAAAGGAGAAAGA GGGGCTCCGGNTGANAAAGGTGAAGGAGGCCCTCCTGNATTGGCAGGGGCCCCANGACTT AGAGGTGGAGCTGGCCCCCCTGGCCCCGAAGGAGGAAAGGGTGCTGCTGGTCCTCCTGGG CCACCTGG 87 / 92

## 16524.2.edit

TCGAGCGGCCCCGGGCAGGTCTGGGCCAGGAGGACCAATAGGACCAGTAGGACCCCTT GGGCCATCTTTCCCTGGGACACCATCAGCACCTGGACCGCCTGGTTCACCCTTGTCACCCTT TGGACCAGGACTTCCAAGACCTCCTCTTTCTCCAGGCATTCCTTGCAGACCAGGAGTACCA NCAGCACCAGGTGGCCCAGGAGGACCAGCAGCACCCTTTCCTCCTCTCGGGACCAGGGGGA CCAGCTCCACCTCTAAGTCCTGGGGCCCCTGCCAATCCAGGAGGGCCTCCTTCACCTTTCTC

#### 16526.1.edir

TCGAGCGGCCGCCCGGGCAGGTCCACCGGGATATTCGGGGGGTCTGGCAGGAATGGGAGGCATCCAGAACGACGACGAGAACGAAGGAGACCATGCAAAGCCTGAACGACCGCCTGGCCTCTTACCTGGACAGAGTGAGGAGCCTGGAGACCAAAATCCGGGAGCACTTGGAGAGAAAAATCCGGGAGCACTTGAGAGAAAAATCCGGGAGCACTTGAGAGAAAAATCATCGAGGACCTGAGGGCCATTACTTCAAGATCATCGAGGACCTGAGGGCCTCANATCTTCGCAAATACTGCNGAGAATGCCCG

#### 16526.2.edit

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NANTTACGGNCATTGCCAATCTGCAGAACGATGCGGGCATTGTCCGCANTATTTGCGAAG
ATCTGAGCCCTCAGGNCCTCGATGATCTTGAAGTAANGGCTCCAGTCTCTGACCTGGGGTC
CCTTCTTCTCCAAGTGCTCCCGGATTTTGCTCTCCAGCCTCCGGTTCTCCAAGNCT
TCTCACTCTGTCCAGCAAAAGAGGCCAGGCGGNCGATCACGGCTTTTGCATGGACT

#### 16527, Ledit

## 16527.2.edit

TCGAGCGGCCGCCGGGCAGGTCTGCCAACACCAAGATTGGCCCCCGCCGCATCCACACA GTTNGTGTGCGGGGAGGTAACAAGAAATACCGTGCCCTGAGGNTGGACGNGGGGAATTTC TCCTGGGGCTCAGAGTGTTGTACTCGTAAAACAAGGATCATCGATGTTGTCTACAATGCAT CTAATAACGAGCTGGTTCGTACCAAGACCCTGGTGAAGAATTGCATCGTGCTCATNGACA GCACACCGTACCGACAGTGGGTACCGAAGTCCCACTATGCNCCT

TCGAGCGGCCGCCCGGGCAGGTCCACCACCCAATTCCTTGCTGGTATCATGGCAGCCGC CACGTGCCAGGATTACCGGCTACATCATCAAGTATGAGAAGCCTGGGTCTCCTCCCAGAGA AGTGGTCCCTCGGCCCCGCCCTGGTGTCACAGAGGCTACTATTACTGGCCTGGAACCGGGA ACCGAATATACAATTTATGTCATTGCCCTGAAG

## 16528.2.edit

AGCGTGNTCNCGGCCGAGGATGGGGAAGCTCGNCTGTCTTTTTCCTTCCAATCAGGGGCTN
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CCAGTAATAGTAGCCTCTGTGACACCCAGGGCGGGGCCGAGGGACCACTTCTCTGGGAGGA
GACCCAGGCTTCTCATACTTGATGATGAAGCCGGTAATCCTGGCACGTGGGCGGCTGCCAT
GATACCACCAANGAATTGGGTTGGTGGACCTGCCCGGGCGGCCGCTCGAAAANCCGAA
TTCNTGCAAGAATATCCATCACACTTGGGCGGGCCGNTCGAACCATGCATCNTAAAAGGG
CCCCAATTTCCCCCCCTATTAGGNGAAGCCNCATTTAACAAATTCCACTTGG

## 16529.1.edit

## 16529.2.edit

## 16530.2.edit

## 16531.1.edit

## 16531.2.edit

AGCGTGGTCGCGGCCGAGGTCTGTACTCGGAGCTAAGCAAACTGACCAATGACATTGAAG
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CCATCCTCCCTCCCAGCCCCACAATTATGGCTGCTGGCCCTCTCCTGGTACCATTCACCCT
CAACTTCACCATCACCAACCTGCAGTATGGGGAGGACATGGGTCACCCTGNCTCCAGGAA
GTTCAACACCACA

## 16532.1.edit

# 01\_16558.3.edit

AGCGTGGTCGCGGGCCGAGGTGAGCCACAGGTGACCGGGGCTGAAGCTGGGGCTGCTGGNC

## 02\_16558.4.edit

CAGCNGCTCCNACGGGGCCTGNGGGACCAACAACACCGTTTTCACCCTTAGGCCCTTTGGC
TCCTCTTTCTCCTTTAGCACCAGGTTGACCAGCAGCNCCANCAGGACCAGCAAATCCATTG
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CT

# 03\_16535.1.edit

TCGAGCGGTCGCCCGGGCAGGTCCACCGGGATAGCCGGGGGTCTGGCAGGAATGGGAGGC ATCCAGAACGAGAAGGAGACCATGCA4AGCCTGAACGACCGCCTGGCCTCTTACCTGGAC AGAGTGAGGAGCCTGGAGACCGGANAACCGGAGGCTGGANAGCA4AATCCGGGAGCACTT GGAGAAGAAGGGACCCCAGGTCA4GAGACTGGAGCCATTACTTCAAGATCATCGAGGGA CCTGGAGG

# 04\_16535.2.edit

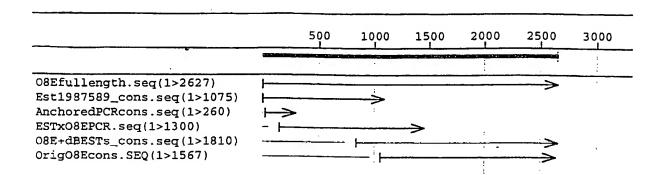
# 05\_16536.1.edic

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# 07\_16537.1.edit

## 08\_16537\_2 edit

TCGAGCGGTCGCCCGGGCAGGTTTCGTGACCGTGACCTCGAGGTGGACACCACCCTCAAG
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TGACCCCAACCAAGGCTGCAACCTTGGATGCCATCAAAGTCTTCTGCAACATGGAGACTGGT
GAGACCTGCGTGTACCCCACTCAGCCCAGTGTGGGCCCAGAAGAAACTTGGTACATCAGCA
AGGAACCCCAAGGACAAGAGGCATTGTCTTGGTTCGGCGAGMAGCATGACCCGATGGATT
CCAGTTTCGAGTATTGGCGGCCAGGGCTTCCCCGACCCTTGCCGATGGACCTCGGCCGCG
ACCACCGCT



THIS FAGE BLANK (USPTO)